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Skin disorders in patients with diabetes mellitus: a review

Diabetes mellitus (DM) is a frequent metabolic disease whose prevalence is estimated to be around 9.3 % in the world population in the age group 20—79, corresponding to 463 million affected subjects. Moreover, this prevalence will probably increase in the course of the next years. It accounts for more than 90% of the diabetic patients. Besides systemic complications, those ay also be observed in dermatology. According to the region, the prevalence of skin disorders in patients suffering DM is ranging from 35.4 to 98.8 %. This makes these symptoms a frequent cause of consultation in dermatological practice. The most occurring disorders are skin infections, but yellow nails, candidiasis, acrochordons, limited joint mobility and idiopathic guttate hypomelanosis may also be frequently observed. Diabetic dermopathy and diabetic foot syndrome are also common, such as pigmentation disorders such as acanthosis nigricans and vitiligo.

Differences between patterns of lesions remain unclear among types of DM (type 1 or type 2). Overall, cutaneous infection and xerosis showed to be highly prevalent and important skin disorders in several studies, regardless DM type. Among cutaneous infections, fungal aetiology appears to be the most common and those with bacterial origin are the less frequent.

DM affects the skin through several mechanisms — High levels of glycaemia strongly affect skin homeostasis by impairing the normal functioning of keratinocytes in vitro, decreasing their proliferation and differentiation. They also lead to advanced glycation end products (AGEs) formation. The latter are formed from glycation of proteins, lipids and nucleic acids. They have various deleterious effects at skin levels: inducing reactive oxygen species (ROS) formation, impairing ROS clearance, as well as intra and extracellular proteins function, and inducing pro inflammatory cytokine through nuclear factor κβ (NF-κβ) pathway. AGE alters collagen properties, decreasing flexibility and solubility and increasing its rigidity, thickening dermal collagen, with increased cross linking from non-enzymatic glycosylation, participating in the development of fibrosis. In diabetic patients, the vascular changes found in the skin are similar to those caused by UV-exposure, i.e. thickening of the vessels walls, increasing from thigh to foot and most marked in the capillaries and leading to failure of vascular responsiveness

This paper is aimed to summarize all these pathologies, reporting their prevalence, giving a brief description of the symptoms, of their pathogenesis and guidelines for their management. Dermatologists have a key role in their treatment, but also in detecting new cases of DM when taking in charge these pathologies. They must also promote glycaemic control by these patients.

Keywords

Diabetes mellitus, prevalence, skin infections, diabetic dermopathy, diabetic foot.

An estimated 463 million adults aged 20—79 years are currently living with diabetes. This represents 9.3 % of the world's population in this age group. The total number is predicted to rise to 578 million (10.2 %) by 2030 and to 700 million (10.9 %) by 2045 [1]. Additionally, about 77 % of people with diabetes live in less developed regions [1].

Diabetes mellitus (type 2 diabetes) is the most common type of diabetes, accounting for around 90 % of all diabetes worldwide [1].

Besides life-threatening acute diabetes complications, chronic complications may also occur, being mainly renal, vascular or ophthalmic.

A broad spectrum of skin disorders can be observed in diabetic patients, which will be reviewed in this paper.

1. Epidemiology of skin disorders in diabetes mellitum

Several epidemiological studies were performed worldwide in order to assess the frequency of skin disorders in patients with diabetes mellitus (DM).

The results of the reviewed studies are varying according to the region, from 35.4 to 98.8 %. Our review was limited to publications from 2000 onward. Previously, one author was assessing that 100 % of diabetic patients have skin involvement [2].

In a study including one hundred and fifty-one type 2 diabetic patients, the overall prevalence of one or more identifiable/apparent skin conditions was 85.4 % [3].

In another report, among 278 patients with DM, 63.1 % presented skin disorder(s) [4].

Table 1. **Prevalence of skin disorders in patients with DM**

Year	Authors	Country	N patients	Prevalence of skin disorders
2006	Sasmaz et al. [3]	Turkey	151	85.4 %
2005	Foss et al. [4]	Brazil	278	63.1 %
2007	da Silva et al. [5]	Brazil	55	89.1 %
2010	Farschian et al. [6]	Iran	155	71.0 %
2010	Goyal et al. [7]	India	100	57.44 %
2011	Ragunatha et al. [8]	India	500	98.8 %
2013	Galdeano et al. [9]	Argentina	125	35.4 %
2014	Wambier et al. [10]	Brazil	500	45.5 %
2014	Chatterjeee et al. [11]	India	680	75.61 %
2014	Sawatkar et al. [12]	India	500	67.8 %
2020	Sani et al. [13]	Nigeria	100	72.0 %

A Brazilian investigation on 55 patients with DM showed skin abnormalities in 89.1 % of them [5]. In Iran, Farschian et al. examined 155 patients with DM and found that the prevalence of skin lesions was 71.0 %, emphasizing on that in their series, such manifestations were more prevalent in patients with DM than in those with type 1 diabetes [6]. In an Indian investigation, one hundred consecutive patients were reviewed, of them 57.44 % were presenting at least one dermatological symptom [7]. Still in India, a total of 500 consecutive patients were studied in a tertiary care hospital. DM was affecting 98.8 % (494/500) of patients. Cutaneous disorders specific to diabetes were present in 257 (51.1 %) patients with DM [8]. In Argentina, a study included 125 diabetic patients. Among them, 88 % were suffering DM. Of them, 35.4 % had at least one symptom of diabetic dermopathy [9]. Back to Brazil, in a randomly chosen sample of 500 DM patients, prevalence of skin disorder was 45.5 % [10]. In India again, six hundred and eighty (680) diabetic patients were examined and 95.3 % of them had DM. Among DM patients, 490 (75.61 %) showed skin lesions [11]. Still in India, clinical examination and relevant investigations were done in 500 subjects with DM. It could be observed that 339 (67.8 %) of them had one or more dermatoses [12]. More recently, one hundred consecutive diabetic patients attending a clinic were included in a study in Nigeria. Seventy-two (72 %) of the subjects had diabetes mellitus. The prevalence of skin diseases was 61 % among these patients [13]. Altogether, in these studies a total of 3144 patients were enrolled, and the mean prevalence of skin disorders was 70.35 %, ranging from 35.4 to 98.8 %. These results are summarized in Table 1.

2. Which are theskin disorders more prevalent in patients with DM?

This information may be extracted from the studies previously mentioned, but also from other publications that we have reviewed. Table 2 is giving an exhaustive summary of our conclusions. Among this review, 6 authors (50 %) [3, 4, 6, 10, 11, 14] mention cutaneous infection as the most prevalent skin disorder in DM patients. In four more studies (33.3 %) [5, 8, 9, 13] this condition is the second most frequent one and in one study [7] it takes the third position. When cutaneous infection is not the most common skin concern, this is xerosis in two cases [7, 9], followed by yellow nails and candidiasis [5], acrochordon [8], limited joint mobility [12] and idiopathic guttate hypomelanosis[13]. Other less prevalent disorders frequently include diabetic dermopathy [7, 9, 12—14] but also pigmentation disorders such as vitiligo or acanthosis nigricans [8, 10, 14]. Altogether the most common dermatological abnormalities are cutaneous infections, xerosis and diabetic dermopathy.

Differences between patterns of lesions remain unclear among types of DM (type 1 or type 2) [15]. Overall, cutaneous infection and xerosis showed to be highly prevalent and important skin disorders in several studies, regardless DM type [15]. Among cutaneous infections, fungal aetiology appears to be the most common and those with bacterial origin are the less frequent.

3. Aetiology of skin disorders in DM

Skin disorders in DM patients are highly correlated with defective glycaemic control [15].

Table 2. **Most frequent skin disorder in patients with DM**

Year	Authors	Country	N patients	Most frequent skin disorder (%)	Other disorders observed (%)
1998	Romano et al. [14]	Italy	457	Cutaneous infections (20 %)	Diabetic dermopathy (12.5 %) Vitiligo (9 %)
2006	Sasmaz et al. [3]	Turkey	151	Cutaneous infection (31.7 %)	Intertrigo (20.5 %) Eczema (15.2 %)
2005	Foss et al. [4]	Brazil	278	Cutaneous infection (82.6 %)	Actinic degeneration (66.7 %) Xerosis (20.6 %)
2007	da Silva et al. [5]	Brazil	55	Yellow nails (52.7 %) Candidiasis (52.7 %)	Cutaneous infections (50.9 %)
2010	Farschian et al. [6]	Iran	155	Cutaneous infections (72 %)	
2010	Goyal et al. [7]	India	100	Xerosis (44 %)	Diabetic dermopathy (36 %) Cutaneous infections (31 %)
2011	Ragunatha et al. [8]	India	500	Acrochordon (26 %)	Cutaneous infections (20.6 %) Acanthosis nigricans (5 %)
2013	Galdeano et al. [9]	Argentina	125	Xerosis (69 %)	Cutaneous infections (52.8 %) Diabetic dermopathy (35 %)
2014	Wambier et al. [10]	Brazil	500	Cutaneous infections (52 %)	Xerosis 28 % Pigmentation disorders (25 %)
2014	Chatterjeee et al. [11]	India	680	Cutaneous infections (63.4 %)	Xerosis (34.8 %) Loss of hair (27 %)
2014	Sawatkar et al. [12]	India	500	Limited joint mobility (16.8 %)	Xerosis (15.8 %) Diabetic dermopathy (10 %)
2020	Sani et al. [13]	Nigeria	100	Idiopathic guttate hypomelanosis (61 %)	Cutaneous infection (30 %) Diabetic dermopathy (17 %)

DM affects the skin through several mechanisms:

- High levels of glycaemia strongly affect skin homeostasis by impairing the normal functioning of keratinocytes in vitro, decreasing their proliferation and differentiation [16, 17].
- They also lead to advanced glycation end products (AGEs) formation. The latter are formed from glycation of proteins, lipids and nucleic acids [18, 19]. They have various deleterious effects at skin levels: inducing reactive oxygen species (ROS) formation, impairing ROS clearance, as well as intra and extracellular proteins function, and inducing pro inflammatory cytokine through nuclear factor κβ (NF-κβ) pathway [20].
- AGE alters collagen properties, decreasing flexibility and solubility and increasing its rigidity, thickening dermal collagen, with increased cross linking from non-enzymatic glycosylation, participating in the development of fibrosis.
- In diabetic patients, the vascular changes found in the skin are similar to those caused by UV-exposure, i.e. thickening of the vessels walls, increasing from thigh to foot and most marked in the capillaries and leading to failure of vascular responsiveness [2].

4. Skin disorders strongly associated with diabetes mellitum

4-1 Acanthosis nigricans

Epidemiology

Acanthosis nigricans (AN) is a common skin manifestation occurring in DM patients, men or women, at any age. It was reported to be more frequent in type 2 DM [22] and most commonly occurs in Native Americans, African Americans, Hispanics and Caucasians]23]. AN prevalence is currently on the rise due to increase in obesity and diabetes in the population. Prevalence varies from 7—74 % in population depending on age, race, type of AN, degree of obesity and associated endocrine issues [23].

Clinical patterns

It features multiple poorly demarcated plaques with grey to dark-brown hyperpigmentation and a thickened velvety to verrucous texture [24]. They are usually symmetrically distributed over the face, neck, axillae, external genitalia, groin, medial thighs, popliteal and antecubital fossae, knuckles, umbilicus or anus [25].

Pathogenesis

The pathogenesis of AN is not completely understood and it is thought that a hyperinsulin state activates insulin growth factor receptors (IGF), specifically IGF-1, in keratinocytes and fibroblasts, provoking cell proliferation, resulting in the clinical features of AN [26].

Treatment

Lifestyle changes such as dietary modifications, increased physical activity, and weight reduction usually improve the symptoms of AN [24]. Common topical treatments include retinoids, topical Vitamin D analogues and keratolytics [25]. Trichloracetic acid (TCA) peelings have also been successfully used in this indication [25]. Systemic treatments such as retinoids are also useful [25]. Metformin, improving glycaemic control and reducing insulin resistance, may also be beneficial [27].

4-2 Diabetic dermopathy

Epidemiology

Diabetic Dermopathy (DD) constitutes one of the most common dermatologic manifestations of diabetes. Its incidence may range from 7 to 70 % of diabetic patients [28]. Although disputed, some consider the presence of DD to be pathognomonic for diabetes [24]. The preferred target of DD are men over 50 [29].

Clinical patterns

DD consists of small, well-defined surface, brownish depressions, with atrophic appearance, resembling scars. Commonly the lesions measure less than 1cm in diameter and present rounded shape. They can occasionally extend and reach up to 2.5 cm [28]. The pretibial area is most commonly involved, although other bony prominences such as the forearms, lateral malleoli or thighs may also be involved [24]. Histologically, DD is characterized by lymphocytic infiltrates surrounding vasculature, engorged blood vessels in the papillary dermis, and dispersed hemosiderin deposits [24].

Pathogenesis

The aetiology of DD remains unclear, mild trauma to affected areas, hemosiderin and melanin deposition, microangiopathic changes and destruction of subcutaneous nerves have all been suggested [24].

Treatment

Treatment of DD is not recommended, given their self-resolving nature as well as the ineffectiveness of available treatments [24].

4-3 Diabetic Foot Syndrome

Epidemiology

Diabetic Foot Syndrome (DFS) designs the neuropathic and vasculopathic complications that develop in the feet of patients with diabetes. Although preventable, DFS is a significant cause of morbidity, mortality, hospitalization, and reduction in quality of life of patients with diabetes [24]. About 25 % of diabetics may present foot ulcers during the development of disease [30] and the incidence and prevalence of DFS in patients with diabetes is 1 to 4 % and 4 to 10 %, respectively [31].

Clinical patterns

In diabetic neuropathy, callosities and dry skin usually occur and may lead to ulcers in areas prone to trauma, classically presenting at the site of calluses or over bony prominences, for instance toes, forefoot, lower legs and ankles [24]. These ulcers may likely be complicated by fungal infections, leading to gangrenous necrosis and may require lower limb amputation.

Pathogenesis

Diabetic ulcers are due to a combination of various factors: diabetes neuropathy (60—70 %) and in a much smaller proportion is linked to peripheral vascular ischemia (about 15 %) [28]. Impaired wound healing is also of concern in the occurrence of this disorder.

Treatment

These ulcers are difficult to heal, and their management must involve a multidisciplinary team including general surgery, vascular surgery, orthopaedics, endocrinology and dermatology. Prevention is of importance and entails daily surveillance, appropriate foot hygiene, and proper footwear, walkers, or other devices to minimize and distribute pressure [24]. Wound dressing (hydrogels) and hyperbaric oxygen therapy are the first-line treatment. Occurrence of infection is at high risk and regular controls are necessary. In case of occurrence, systemic antibiotherapy will be required.

4-4 Scleroderma-like skin changes

Epidemiology

Scleroderma-like skin changes (SLSC) are commonly observed in patients with diabetes and its prevalence is quoted as 10—15 % by certain authors [32] as others consider that it can occur in up to 50 % of the patients with type 1 diabetes [28]. No known variation in prevalence between males and females, or between racial groups were reported [24].

Clinical patterns

It features thickening and hardening of the skin of the dorsal region of the finger as well as the skin overlying the joints of the hand and fingers. These changes are more common in type 1 diabetes and occur in up to 50 % of the patient [28]. Some patients with diabetes may develop more extensive disease, presenting earlier and with truncal involvement named Sclerederma diabeticorum, or Scleredema Adultorum of Buschke (SAB). It is characterized by symmetrical and diffuse thickening with hardening of the skin affecting mainly the face, trunk, neck and upper limbs, sparing the hands and feet [33]. DM is associated with about 50 % of cases and its prevalence varies between 2.5 and 14 % in diabetic patients [34].

Pathogenesis

Histopathology shows marked thickening of the reticular dermis with thick collagen bundles separated by bands of hyaline deposit, mucin or hyaluronic acid [28]. Hardening and thickening of collagen is believed to be a result of reactions associated with advanced glycosylation end products or a build-up of sugar alcohols in the upper dermis [35].

Treatment

There are very few therapeutic options. It was suggested that aldose reductase inhibitors, by limiting increases in sugar alcohols, could be efficacious [35].

4-5 Limited joint mobility

Epidemiology

The prevalence of Limited Joint Mobility (LJM) is 4 to 26 % in patients without diabetes and 8 to 58 % in patients with diabetes [36].

Clinical patterns

LJM presents with progressive flexed contractures and hindered joint extension, most commonly involving the metacarpophalangeal and interphalangeal joints of the hand [24] which makes that these patients are unable to flushly press the palmar surfaces of each of their hands together («prayer sign»). This is a result of periarticular enlargement of connective tissue.

Pathogenesis

As in SLSC, hyperglycaemia-induced formation of advanced glycation end-products, which accumulate to promote inflammation and the formation of stiffening cross-links between collagen are responsible for this disorder [37].

Treatment

There are no curative treatments. Symptomatic patients may benefit from non-steroidal anti-inflammatory drugs or targeted injection of corticosteroids [37]. Regular hand stretching is also recommended [24].

4-6 Necrobiosis lipoidica

Epidemiology

Necrobiosis lipoidica (NL) is an idiopathic dermatosis occurring mainly in patients with diabetes. Its incidence ranges from 0.3 to 1.6 % of these patients per year [38]. NL predominates in women (80 % of cases), mostly white, and it prevails between the fourth and sixth decades [39]. Confirmed diagnosis of diabetes, abnormal plasma glucose or a family history of diabetes occurred in 90 % of patients [39].

Clinical patterns

Once it occurs, NL features a single firm well-demarcated rounded erythematous papule. Then they multiply, expand and aggregate into plaques characterized by circumferential red-brown borders and a firm yellow-brown waxen atrophic centre containing telangiectasias [24]. NL affects preferably legs and usually develops symmetrically on both legs and exhibits Koebnerization. Patients occasionally present itching or burning sensations in areas where the disease is asymptomatic, approximately 35 % of the lesions progress to ulceration and pain arises after ulceration [40].

Pathogenesis

Histopathology shows disorganization and degeneration ofcollagen in basement membrane thickening and inflammation of theunderlying subcutaneous fat [28].

Pathogenesis of NL is unclear, and microangiopathy, defects in collagen or autoimmune disease have been evoked.

Treatment

Spontaneous resolution is observed in 10 to 20 % of cases, sometimes after many years [24, 28]. In general, drug treatment has little effect and should be reserved for symptomatic relief. Intralesional injection and oraluse of corticosteroids or topical threads under occlusion, clofazimine,acetylsalicylic acid, dipyridamole, pentoxyphiline and chloroquine are used with irregular success [28].

4-7 Bullosis diabeticorum

Epidemiology

The prevalence of Bullosis diabeticorum (DB) is around 0.5 % in patients with DM [14]. BD has been reported in patients aged 17 to 80 years, age of onset is preferably between 50 and 70, with a larger proportion in males (2 : 1) [41].

Clinical patterns

Occurrence of BD features the sudden onset of one or more non-erythematous, firm, sterile bullae. Shortly after forming, bullae increase in size and become more flaccid, ranging in size from about 0.5 to 5 cm [24]. Blisters are often bilateral, with an inflammatorybase, and contain a clear, sterile, nonserous content [42]. They preferably involve involving the acral areas of the lower extremities but may also affect the back and side of the hands and the arms [42]. They are usually painless and non-pruritic and disappear spontaneously without scarring after 2—6 weeks [42].

Pathogenesis

Pathophysiology of the BD is still unknown. Autoimmune processes, exposure to ultraviolet light, variations in blood glucose, neuropathy, or changes in microvasculature have been proposed [43].

Treatment

There is no need for specific treatment of BD, and the spontaneously resolve.

Protection of the affected skin and leaving blisters intact must be recommended to the patients, to avoid secondary infection.

4-8 Hydradenitis suppurativa

Epidemiology

The most recent study of hidradenitis suppurativa (HS) epidemiology based upon primary healthcare data demonstrates a prevalence of less than 1 % [44]. HS is more prevalent in women than men and usually occurs in patients beginning in their twenties [45]. Compared to the general population, diabetes mellitus is three-times more common in patients with HS than in general population [46].

Clinical patterns

HS is a chronic inflammatory disease affecting apocrine gland bearing skin. It is characterized by inflamed, painful and malodorous nodules and abscesses located in areas such as the axilla or groin. It can lead to the development of disfiguring scars.

Pathogenesis

Hidradenitis suppurativa is a complex disorder whosepathogenesis is unclear at present [47]. Histopathology showsthat the primary event is follicular occlusion whereinfundibular hyperkeratosis of the terminal follicles andhyperplasia of the follicular epithelium result in the collection of cellular debris, cyst formation, rupture, sinus tractformation and ultimately, scarring [48]. Disruption of the hair follicle produces a significant inflammatory response, recruiting self-perpetuating inflammatory mediators [49]. Contributing factors to the inflammatory drive in hidradenitissuppurativa include the patient's genotype, smoking habit, obesity, adipokine dysregulation, insulin or glucose dysregulation, the microbiome and environmental factors [49].

Treatment

Some benefits have been reported with the use of antibiotics, retinoids, antiandrogens, metformin, immunomodulators (IL-1, -12, -17 and -23 inhibitors, TNF-α inhibitors, Janus-kinase inhibitors, methotrexate or cyclosporine) [24, 50].

5. Non-specific dermatological signs and symptoms

5-1 Ichthyosiform changes of the shins

Epidemiology

The prevalence of ichthyosiform changes of the shins (ICS) in those with type 1 diabetes has been reported to be between 22 to 48 % [51, 52] with no difference between male and females.

Clinical patterns

ICS feature large bilateral areas of dryness and scalingoccurring preferably on the hands or feet, the anterior shin beingalso classically involved [24]. ICS are related to rapid skin aging and adhesion defects in the stratum corneum [53].

Pathogenesis

ICS are the result of production of advanced glycosylation end products and microangiopathic changes [24].

Treatment

Topical emollients or keratolytic agents may be beneficial [53].

5-2 Xerosis

Epidemiology

Xerosis is one of the most common and prevalent presentations in DM. As mentioned in chapter 2, it may affect up to 69 % of patients with DM [9].

Clinical patterns

Xerosis features abnormally dry skin, presenting with scaling, cracks or a rough texture, most frequently located on the feet and susceptible of worsening to diabetic foot syndrome.

Treatment

Emollients are the first line treatment of xerosis.

5-3 Acquired perforating dermatosis

Epidemiology

Acquired perforating dermatosis (APD) is commonly observed in patients with long-standing diabetes, usually occurring between the ages of 30 and 90 years of age [54]. APD may also present in patients with renal failure.

Clinical patterns

APD present as groups of hyperkeratotic umbilicated-nodules and papules with centralized keratin plugs and undergoing Koebnerization [24]. Arms and legs are the most commonly affected, but they can also appear on other parts of the body, especially on the trunk [24]. Lesions are extremely pruritic and are aggravated by excoriation.

Pathogenesis

The pathogenesis of APD is poorly understood. Repetitive chronic scratching and the glycosylation of microvasculature or dermal components have been evoked.

Treatment

Minimizing scratching may improve the lesions, hence the symptomatic relief of pruritus may be recommended. Individual lesions can be managed with topical agents such as keratolytics (e.g. 5 to 7 % salicylic acid), retinoids (e.g. 0.01 to 0.1 % tretinoin), or high-potency steroids whilst refractory lesions may respond to intralesional steroid injections or cryotherapy [55]. A reasonable initial approach is a topical steroid in combination with emollients and an oral antihistamine [24].

If this treatment does not bring successful result, a systemic approach may be necessary combining oral retinoids, psoralen plus UVA light (PUVA), allopurinol (100 mg daily for 2 to 4 months), or oral antibiotics (doxycycline or clindamycin) [56].

5-4 Eruptive xanthomas

Epidemiology

The prevalence of EX was reported as being around 1 % in type 1 diabetes and 2 % in type 2 diabetes [57].

Clinical patterns

Eruptive xanthomas (EX) features eruptions of clusters of glossy pink-to-yellow papules, ranging in diameter from 1 mm to 4 mm, overlying an erythematous area most often occurring on the extensor surfaces of the extremities or the buttocks [24]. They are commonly asymptomatic.

Pathogenesis

In an insulin deficient state such as DM, there is decreased lipoprotein lipase activity resulting in the accumulation of triglyceride rich lipoproteins in the tissues, among them in the skin, which will be scavenged by macrophages which may collect in the dermis and lead to EX [58].

Treatment

EX may resolve with a better control of diabetes and triglyceride levels, for instance by oral intake of fibrates and omega-3-fatty acids [24].

5-5 Acrochordons

Epidemiology

Acrochordons, also named skin tags, are a frequent presentation in patients with DM. Their prevalence may reach up to 26 % [8].

Clinical patterns

Acrochordons feature benign, soft, pedunculated growths varying in size occurringisolated or in collections. They affect preferably the neck, axilla, and periorbital area.

Treatment

Usually acrochordons are not treated, but in those who feel affected in term of cosmetic appearance and self-esteem, excision or cryotherapy may be performed.

5-6 Diabetes-associated pruritus

Epidemiology

In 1986 300 diabetic and 100 nondiabetic hospital outpatients were assessed for the presence of generalized and localized pruritus. In the diabetic group, 13 patients (4.33 %) complained of generalized pruritus vs. 1 % in control group.

The prevalence of localized pruritus washigher in the nondiabetic control group (10 %) than in thediabetic group (7.7 %) without significant difference.

An interesting finding was that Pruritus vulvae wassignificantly more common in diabetic women (18.4 %) than in controls (5.6 %) and was significantlyassociated with poor diabetes control [59].

Clinical patterns

As mentioned above, pruritus in diabetic patients is more often localized than generalized and affected areas can include the scalp, ankles, feet, trunk, or genitalia, more likely in patients who have dry skin or diabetic neuropathy.

Treatment

Treatments are classical protocols for pruritus including topical capsaicin, topical ketamine-amitriptyline-lidocaine, oral anticonvulsants (e.g. gabapentin or pregabalin) [24].

5-7 Huntley's papules

Epidemiology

In 1986, when Huntley described this disorder, he evaluated the incidence of these «finger pebbles» in diabetic patients in a case-controlled studyin 112 subjects and reported that approximately 75 % ofpatients with diabetes mellitus have a visual marker of skin hypertrophy on their fingers, whilst these changesoccur in only 21 % of nondiabetic individuals [60]. Another paper reported a rate of finger pebbles of 72 % in 202 diabetic patients vs. only 12 % in 48 healthy subjects; the prevalence of this manifestation was similar in menand women, did not vary with age, and, as in Huntley's data,was higher in patients with type II diabetes [61].

Clinical patterns

Huntley's papules are represented by a velvety patternsimilar to that observed on the knuckle and periungual skin ofmanual laborers, or on the radial side of the third digit of thedominant hand as a result of holding a pen [62].

Pathogenesis

Although the exact pathogenesis is unknown, the non-enzymatic glycoxidation of collagen could well be the basic pathophysiologic mechanism [62].

Treatment

Application of emollients is the only treatment which should be recommended in this case.

5-8 Keratosis pilaris

Epidemiology

In a study, keratosis pilaris (KP) was found to be present in 21 % of the patients with DM versus 9 % in control subjects [51].

Clinical patterns

Keratosis pilaris classically presents with areas of keratotic perifollicular papules with surrounding erythema or hyperpigmentation. The posterior surfaces of the upper arms are often affected but the thighs, face and buttocks can also be affected [24].

Pathogenesis

The most accepted theory of its pathogenesis proposes defective keratinization of the follicular epithelium resulting in a keratotic infundibular plug. In case of DM, this is probably a consequence of the deleterious action of high levels of glycaemia on the keratinocytes.

Treatment

Topical therapies, including salicylic acid, moisturizers, and emollients are the first line treatment of KP.

5-9 Yellow skin and nails

Epidemiology

This pattern is common in DM patients. In a previously mentioned study, it was even the most frequent skin disorder in the group of patients under study with 52.7 % of prevalence [5]. It particularly affects elderly patients.

Clinical patterns

This pattern presents with asymptomatic yellow discolorations of skin or finger nails commonly involving the palms, soles, face, or the distal nail of the first toe [24].

Pathogenesis

As in other syndromes associated with DM, the accumulation of glycosylated proteinsmay be responsible for these changes; however, the pathogenesis remains controversial.

Treatment

There is no specific treatment for this disorder.

5-10 Generalized Granuloma Annulare

Epidemiology

It was reported that 10—15 % of cases of GGA occur in patients with diabetes, i.e. its prevalence in DM is higher than in the general population [28]. GGA occurs around the average age of 50 years. It occurs more frequently in women than in men [28].

Clinical patterns

The cutaneous lesions are similar to necrobiosis lipoidicadiabeticorum, but without causing atrophy of the epidermis [63]. It is characterized by papules that often assume an annular configuration.

Pathogenesis

The probable pathophysiology is a stimulus that triggers the release of lymphokines by previously activated lymphocytes. These lymphokines stimulate the synthesis and activity of collagenase, producing an inflammatory reaction that modulates the formation of granulomas [63].

Treatment

GGA has a poor therapeutic response. If the patients is requesting a treatment, the therapeutic options include high-dose topical steroids, intralesional injection of corticosteroids, PUVA, cryotherapy, or drugs such as niacinamide, infliximab, dapsone and topical calcineurin inhibitors [64].

6. Cutaneous infections

As aforementioned, cutaneous infections are the most prevalent disorder associated with DM (see chapter 2). These may be of fungal or bacterial origin.

Various factors such as angiopathy, neuropathy, hindrance of the antioxidant system, abnormalities in leukocyte adherence, chemotaxis, and phagocytosis, as well as a glucose-rich environment facilitates the growth of pathogens are favouring the occurrence and repetition of these infections [24].

6-1 Bacterial infections

Bacterial skin infections are common in diabetics and typically include erythrasma, erysipelas, impetigo, folliculitis, multiple abscesses, furuncle, and carbuncle [65].

Erysipelas presents with pain and well-demarcated superficial erythema, whilst **cellulitis** is a deeper cutaneous infection that also presents with pain but with poorlydemarcated erythema [24]. **Folliculitis** is characterized by inflamed, perifollicular, papules and pustules.Uncomplicated cellulitis and erysipelas are treated with oral antibiotics, whereas uncomplicated folliculitis may be managed with topical antibiotics [24]. Antimicrobial resistance of these antibiotics may be of concern in such treatments.

Diabetic foot is also very prone to infections. In such case, Staphylococcal infections are the most common [66], although complications with infection by Pseudomonas aeruginosa are also common. Topical or oral antibiotics and surgical debridement may be indicated depending on the severity of the infection [24].

Necrotizing fasciitis also affects diabetics more frequently than non-diabetics, presenting early with erythema, induration, and tenderness which may then progress within days to haemorrhagic bullous. The most common causal pathogens are Staphylococcus aureus, Streptococcus pyogenes, anaerobic Streptococcus and Bacteroides species [65]. Despite optimal therapy including swift administration of systemic antibiotics, surgical debridement, and ICU monitoring, the mortality rate is 20—30 % [67].

Erythrasma is a chronic asymptomatic cutaneous infection also likely to affect patients with DM and presenting with non-pruritic non-tender clearly demarcated red-brown finely scaled patches or plaques.Treatment options include topical erythromycin or clindamycin [24].

Malignant otitis externa may also develop in diabetics, caused by Pseudomonas aeruginosa and lead to osteitis or meningitis, and takes a lethal course in approximately 50 % of cases [68]. Treatment involves long-term systemic antibiotics with appropriate pseudomonal coverage, hyperbaric oxygen, and possibly surgical debridement [24].

6-2 Fungal infections

Candidiasis is a frequent presentation in patients with diabetes. They can present as thrush, angular cheilitis, candidal balanoposthitis, vulvovaginitis, and paronychia as well as intertriginous candidiasis [68]. They feature white oral mucosal patches that can easily be wiped away, erythema and rhagades. In mucocutaneous candidal infections, local antimycotics are the treatment of first choice. Recalcitrant cases may require systemic antimycotic treatment [65].

Although it remains controversial, **dermatophyteinfections** appear to be more prevalent among patients with DM [69], affecting various regions of the body, more especially the foot with tinea pedis. Treatment may include topical or systemic antifungal medications depending on the severity [24].

Mucormycosismay also be associated with DM. Caused by Rhizopus oryzae, mucormycosis may present in different ways. Rhino-orbital-cerebral mucormycosis is the most common presentation; it develops quickly and presents with acute sinusitis, headache, facial edema, and tissue necrosis [24]. It should be treated urgently with surgical debridement and intravenous amphotericin B.

7. Conclusions

Various cutaneous diseases are caused or may be influencedby systemic disorders and specially by DM. Given the high prevalence of DM, knowledge, diagnosisand treatment of these disorders is of major importancefor the dermatologist.

Besides, early diagnosis of these presentations can help in the early diagnosis of DM and consecutive treatment.Adequate glycaemic control and primary prevention of specific damage to internal organs should be promoted and reinforcedby dermatologists, as they are the base for the improvement of these diseases.

References

1. IDF Diabetes Atlas. 9th edition, 2019.— International Diabetes Federation, Brussels.— 176 p.
2. Huntley A.C. Diabetes and the skin // J. Am. Acad. Dermatol.— 1982.— Vol. 7.— P. 427—455.
3. Sasmaz S., Buyukbese M., Cetinkaya A. et al. The prevalence of skin disorders in type-2 diabetic patients // Internet J. Dermatol.— 2006.— Vol. 3 (1).— 4 p.
4. Foss N.T., Polon D.P., Takada M.H. et al. Dermatoses em pacientes com diabetes mellitus // Revista de Saúde Públic.— 2005.— Vol. 39.— P. 677—682.
5. da Silva MC.A., Mazzotti N.G., Weber M.B. Manifestações cutâneas em pacientes comdiabete melito tipo 2 em posto de saúde // Revista da Associação Médica do Rio Grande do Sul.— 2007.— Vol. 51.— P. 95—99.
6. Farshchian M., Fereydoonnejad M., Yazdanfar A. et al. Cutaneous manifestations of diabetes mellitus: a case series // Cutis.— 2010.— Vol. 86.— P. 31—35.
7. Goyal A., Raina S., Kaushal S.S. et al. Pattern of cutaneous manifestations in diabetes mellitus // Indian J. Dermatol.— 2010.— Vol. 55 (1).— P. 39—41. doi: 10.4103/0019-5154.60349.
8. Ragunatha S., Anitha B., Inamadar A.C. et al. Cutaneous disorders in 500 diabetic patients attending diabetic clinic // Indian J. Dermatol.— 2011.— Vol. 56 (2).— P. 160—164. doi: 10.4103/0019-5154.80409.
9. Galdeano F., Zaccaria S., Parra V. et al. Cutaneous manifestations of diabetes mellitus: clinical meaning // Dermatología Argent.— 2013.— Vol. 16.— P. 117—121.
10. Wambier C.G., Takada M.H., Foss-Freitas M.C. et al. Effects of metabolic control on cutaneous findings in diabetes mellitus // Revista Brasileira de Medicina Interna.— 2014.— Vol. 1.— P. 11—19.
11. Chatterjee N., Chattopadhyay C., Sengupta N. et al. An observational study of cutaneous manifestations in diabetes mellitus in a tertiary care hospital of Eastern India // Indian J. Endocrinol. Metab.— 2014.— Vol. 18.— P. 217—220. doi: 10.4103/2230-8210.129115.
12. Sawatkar G.U., Kanwar A.J., Dogra S. et al. Spectrum of cutaneous manifestations of type 1 diabetes mellitus in 500 South Asian patients // Br. J. Dermatol.— 2014.— Vol. 171.— P. 1402—1406. doi: 10.1111/bjd.13077.
13. Sani H., Abubakar A.B., Bakari A.G. Prevalence and pattern of skin diseases in patients with diabetes mellitus at a tertiary hospital in Northern Nigeria // Niger J. Clin. Prac.— 2020.— Vol. 23.— P. 970—974. doi: 10.4103/njcp.njcp_95_19.
14. Romano G., Moretti G., Di Benedetto A. et al. Skin lesions in diabetes mellitus: prevalence and clinical correlations // Diabetes Res. Clin. Pract.— 1998.— Vol. 39.— P. 101—106. doi: 10.1016/s0168-8227(97)00119-8.
15. Campos de Macedo G.M., Nunes S., Barreto T. Skin disorders in diabetes mellitus: an epidemiology and physiopathology review // Diabetol. Metab. Syndr.— 2016.— Vol. 8.— P. 63. doi: 10.1186/s13098-016-0176-y.
16. Spravchikov N., Sizyakov G., Gartsbein M. et al. Glucose effects on skin keratinocytes: implications for diabetes skin complications // Diabetes.— 2001.— Vol. 50.— P. 1627—1635. doi: 10.2337/diabetes.50.7.1627.
17. Chen X.F., Lin W.D., Lu S.L. et al. Mechanistic study of endogenous skin lesions in diabetic rats // Exp. Dermatol.— 2010.— Vol. 19.— P. 1088—1095. doi: 10.1111/j.1600-0625.2010.01137.x.
18. Blakytny R., Jude E.B. Altered molecular mechanisms of diabetic foot ulcers // Int. J. Low Extrem. Wounds.— 2009.— Vol. 8.— P. 95—104. doi: 10.1177/1534734609337151.
19. Behm B., Schreml S., Landthaler M., Babilas P. Skin signs in diabetes mellitus // J. Eur. Acad. Dermatol. Venereol.— 2012.— Vol. 26.— P. 1203—1121. doi: 10.1111/j.1468-3083.2012.04475.x.
20. Wilkinson H.N., Hardman M.J. Wound senescence: a functional link between diabetes and ageing? // Exp. Dermatol.— 2021.— Vol. 30.— P. 68—73. doi: 10.1111/exd.14082.
21. Buckingham B.A., Uitto J., Sandborg C. et al. Scleroderma like syndrome and non-enzymatic glycosylation of collagen in children with poorly controlled insulin-dependent diabetes // Pediatr. Res.— 1981.— Vol. 15.— P. 626.
22. Stuart C.A., Gilkison C.R., Smith M.M. et al. Acanthosis nigricans as a risk factor for non-insulin dependent diabetes mellitus // Clin Pediatr (Phila).— 1998.— Vol. 37 (2).— P. 73—79. doi: 10.1177/000992289803700203.
23. Phiske M. An approach to acanthosis nigricans // Indian Dermatol. Online J.— 2014.— Vol. 5 (3).— P. 239. doi: 10.4103/2229-5178.137765.
24. Rosen J., Yosipovitch G. Skin Manifestations of Diabetes Mellitus / K.R. Feingold, B. Anawalt, A. Boyce et al., editors // Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-. https://www.ncbi.nlm.nih.gov/sites/books/NBK481900/
25. Das A., Datta D., Kassir M. et al. Acanthosis nigricans: a review // J. Cosmet. Dermatol.— 2020.— Vol. 19 (8).— P. 1857—1865. doi: 10.1111/jocd.13544. PMID: 32516476.
26. Bhagyanathan M., Dhayanithy D., Parambath V. et al. Acanthosis nigricans: A screening test for insulin resistance—An important risk factor for diabetes mellitus type-2 // J. Family Med. Prim. Care.— 2017.— Vol. 6 (1).— P. 43. doi: 10.4103/2249-4863.214961.
27. Higgins S.P., Freemark M., Prose N.S. Acanthosis nigricans: a practical approach to evaluation and management // Dermatol. Online J.— 2008.— Vol. 14 (9).— 2 p.
28. Mendes A.L., Miot H.A., Junior V.H. Diabetes mellitus and the skin // An. Bras. Dermatol.— 2017.— Vol. 92 (1).— P. 8—20. doi: 10.1590/abd1806-4841.20175514.
29. Morgan A.J., Schwartz R.A. Diabetic dermopathy: A subtle sign with grave implications // J. Am. Acad. Dermatol.— 2008.— Vol. 58 (3).— P. 447—451. doi: 10.1016/j.jaad.2007.11.013.
30. Tabor C.A., Parlette E.C. Cutaneous manifestations of diabetes. Signs of poor glicemy control or new onset disease // Postgrad. Med.— 2006.— Vol. 119.— P. 38—44.
31. Amin N., Doupis J. Diabetic foot disease: from the evaluation of the «foot at risk» to the novel diabetic ulcer treatment modalities // World J. Diabetes.— 2016.— Vol. 7 (7).— P. 153. doi: 10.4239/wjd.v7.i7.153.
32. Ahn C., Yosipovitch G., Huang W. Diabetes and the Skin // Callen J., Jorizzo J., Zone J. et al., eds. Dermatological Signs of Systemic Disease.— Edinburgh: Elsevier, 2017.— P. 205—214.
33. Gervini R.L., Lecompte S.M., Pineda R.C. et al. Escleredema de Buschke: relato de dois casos // An. Bras. Dermatol.— 2002.— Vol. 77.— P. 465—472.
34. Sattar M.A., Diab S., Sugathan T.N., Sivanandasingham P., Fenech F.F. Scleredemadiabeticorum: a minor but often unrecognized complication of diabetes mellitus // Diabet Med.— 1988.— Vol. 5.— P. 465—468.
35. Yosipovitch G., Loh K.C., Hock O.B. Medical pearl: Scleroderma-like skin changes in patients with diabetes mellitus // J. Am. Acad. Dermatol.— 2003.— Vol. 49 (1).— P. 109—111. doi: 10.1067/mjd.2003.254.
36. Gerrits E.G., Landman G.W., Nijenhuis-Rosien L. et al. Limited joint mobility syndrome in diabetes mellitus: a minireview // World J. Diabetes.— 2015.— Vol. 6 (9).— P. 1108. doi: 10.4239/wjd.v6.i9.1108.
37. Abate M., Schiavone C., Pelotti P., Salini V. Limited joint mobility in diabetes and ageing: recent advances in pathogenesis and therapy // Int. J. Immunopathol. Pharmacol.— 2010.— Vol. 23 (4).— P. 997—1003. doi: 10.1177/039463201002300404.
38. Lowitt M.H., Dover J.S. Necrobiosis lipoidica // J. Am. Acad. Dermatol.— 1991.— Vol. 25.— P. 735—748. doi: 10.1016/s0190-9622(08)80961-9.
39. Jelinek J.E. The skin in diabetes // Diabet Med.— 1993.— Vol. 10.— P. 201—213. doi: 10.1111/j.1464-5491.1993.tb00048.x.
40. Petzelbauer P., Wolff K., Tappeiner G. Necrobiosis lipoidica: treatment with systemic corticoids // Br. J. Dermatol.— 1992.— Vol. 126.— P. 542—545. doi: 10.1111/j.1365-2133.1992.tb00097.x.
41. Larsen K., Jensen T., Karlsmark T., Holstein P.E. Incidence of

bullosisdiabeticorum — a controversial cause of chronic foot ulceration // Int. World J.— 2008.— Vol. 5 (4).— P. 591—596.
42. Basarab T., Munn S.E., McGrath J. et al. Bullosis diabeticorum. A case report and literature review // Clin. Exp. Dermatol.— 1995.— Vol. 20.— P. 218—220. doi: 10.1111/j.1365-2230.1995.tb01305.x.
43. Lipsky B.A., Baker P.D., Ahroni J.H. Diabetic bullae: 12 cases of a purportedly rare cutaneous disorder // Int. J. Dermatol.— 2000.— Vol. 39 (3).— P. 196—200. doi: 10.1046/j.1365-4362.2000.00947.x.
44. Ingram J.R. Hidradenitis suppurativa prevalence and diseaseassociations using the Clinical Practice Research Datalink. 25th European Academy of Dermatology and Venereology Congress, 2016.— Vienna, Austria, 2016.
45. Von der Werth J., Williams H. The natural history of hidradenitis suppurativa // J. Eur. Acad. Dermatol. Venereol.— 2000.— Vol. 14 (5).— P. 389—392. doi: 10.1046/j.1468-3083. 2000.00087.x.
46. Bui T-L., Silva-Hirschberg C., Torres J., Armstrong A.W. Hidradenitis suppurativa and diabetes mellitus: a systematic review and meta-analysis // J. Am. Acad. Dermatol.— 2018.— Vol. 78(2).— P. 395—402. doi: 10.1016/j.jaad.2017.08.042.
47. Vekic D.A., Frew J.W., Woods J. et al. Adopting the orphan: theimportance of recognising hidradenitis suppurativa as a systemic auto-inflammatory disease // Australas. J. Dermatol.— 2016.— Vol. 57.— P. 69—70. doi: 10.1111/ajd.12287.
48. von Laffert M., Helmbold P., Wohlrab J. et al. Hidradenitis suppurativa (acne inversa): early inflammatory events at terminalfollicles and at interfollicular epidermis // Exp. Dermatol.— 2010.— Vol. 19.— P. 533—537.
49. Vekic D.A., Frew J., Cains G.D. Hidradenitis suppurativa, a review of pathogenesis,associations and management. Part 1 // Australas J. Dermatol.— 2018.— Vol. 59 (4).— P. 267—277. doi: 10.1111/ajd.12770.
50. Lyons A.B., Shabeeb N., Nichol C.L. et al. Emerging medical treatments for hidradenitis suppurativa // J. Am. Acad. Dermatol.— 2020.— Vol. 83 (2).— P. 554—562. doi: 10.1016/j.jaad.2020.04.009.
51. Yosipovitch G., Hodak E., Vardi P. et al. The prevalence of cutaneous manifestations in IDDM patients and their association with diabetes risk factors and microvascular complications // Diabetes Care.— 1998.— Vol. 21 (4).— P. 506—509. doi: 10.2337/diacare.21.4.506.
52. Pavlović M.D., Milenković T., Dinić M. et al. The prevalence of cutaneous manifestations in young patients with type 1 diabetes // Diabetes Care.— 2007.— Vol. 30 (8).— P. 1964—1967. doi: 10.2337/dc07-0267.
53. Patel N., Spencer L.A., English J.C., Zirwas M.J. Acquired ichthyosis // J. Am. Acad. Dermatol.— 2006.— Vol. 55 (4).— P. 647—656. doi: 10.1016/j.jaad.2006.04.047.
54. Saray Y., Seçkin D., Bilezikçi B. Acquired perforating dermatosis: clinicopathological features in twenty-two cases // J. Eur. Acad. Dermatol. Venereol.— 2006.— Vol. 20 (6).— P. 679—688. doi: 10.1111/j.1468-3083.2006.01571.x.
55. Van Hattem S., Bootsma A.H., Thio H.B. Skin manifestations of diabetes // Cleve Clin. J. Med.— 2008.— Vol. 75 (11).— P. 772—774. doi: 10.3949/ccjm.75.11.772.
56. Wagner G., Sachse M.M. Acquired reactive perforating dermatosis // J. Dtsch. Dermatol. Ges.— 2013.— Vol. 11 (8).— P. 723—729. doi: 10.1111/ddg.12131.
57. Mahajan S., Koranne R., Sharma S. Cutaneous manifestation of diabetes melitus // Indian J. Dermatol. Venereol. Leprol.— 2003.— Vol. 69 (2).— P. 105.
58. Naik N.S. Eruptive xanthomas // Dermatol. Online J.— 2001.— Vol. 7 (2).— P. 11.
59. Neilly J.B., Martin A., Simpson N., MacCuish A.C. Pruritus in diabetes mellitus: investigation of prevalence and correlation with diabetes control // Diabetes Care.— 1986.— Vol. 9 (3).— P. 273—275.
60. Huntley A.C. Finger pebbles: a common finding in diabetes mellitus // J. Am. Acad. Dermatol.— 1986.— Vol. 14.— P. 612—617.
61. Cabo H., Woscoff A. Cutaneous manifestations of diabetes mellitus [letter] // J. Am. Acad. Dermatol.— 1995.— Vol. 32.— P. 685.
62. Guarneri C., Guarneri F., Borgia F. et al. Finger pebbles in a diabetic patient: Huntley's papules // Int. J. Dermatol.— 2005.— Vol. 44.— P. 755—756. doi: 10.1111/j.1365-4632.2004.02580.x.
63. Dabski K., Winkelmann R.K. Generalized granuloma annulare: clinical and laboratory findings in 100 patients // J. Am. Acad. Dermatol.— 1989.— Vol. 20.— P. 39—47. doi: 10.1016/s0190-9622(89)70005-0.
64. Sahin M.T., Türel-Ermertcan A., Oztürkcan S. et al. Generalized granuloma annulare in a patient with type II diabetes mellitus: successful treatment with isotretinoin // J. Eur. Acad. Dermatol. Venereol.— 2006.— Vol. 20.— P. 111—114. doi: 10.1111/j.1468-3083.2006.01337.x.
65. Gkogkolou P., Böhm M. Skin disorders in diabetes mellitus // J. Dtsch. Dermatol. Ges.— 2014.— Vol. 12 (10).— P. 847—863. doi: 10.1111/ddg.12424_suppl.
66. Casqueiro J., Casqueiro J., Alves C. Infections in patients with diabetes mellitus: A review of pathogenesis // Indian J. Endocrinol. Metab.— 2012.— Vol. 16 (Suppl. 1).— P. 27—36. doi: 10.4103/2230-8210.94253.
67. Ahmed I., Goldstein B. Diabetes mellitus // Clin. Dermatol.— 2006.— Vol. 24.— P. 237—246. doi: 10.1016/j.clindermatol.2006.04.009.
68. Oumeish O.Y. Skin disorders in patients with diabetes // Clin. Dermatol.— 2008.— Vol. 26.— P. 235—242. doi: 10.1016/j.clindermatol.2007.10.015.
69. Saunte D.M.L., Holgersen J.B., Hædersdal M. et al. Prevalence of toe nail onychomycosis in diabetic patients // Acta Derm. Venereol.— 2006.— Vol. 86 (5).— P. 425—428. doi: 10.2340/00015555-0113.

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Шкірні розлади у пацієнтів із цукровим діабетом: огляд літератури

Цукровий діабет (ЦД) — це часте метаболічне захворювання, поширеність якого оцінюється приблизно в 9,3 % серед населення світу у віковій групі 20—79 років, що відповідає 463 млн хворих. Більше того, захворюваність на цю хворобу, ймовірно, збільшиться протягом наступних років. На її частку припадає понад 90 % хворих на цукровий діабет. Системні ускладнення також можуть спостерігатися в дерматології. Залежно від регіону поширеність шкірних захворювань у хворих на ЦД становить від 35,4 до 98,8 %, що робить ці симптоми частим приводом для консультацій в дерматологічній практиці. Найбільш поширеними захворюваннями є шкірні інфекції, але також часто можуть спостерігатися жовті нігті, кандидоз, акрохордони, обмежена рухливість суглобів і ідіопатичний каплевидний гіпомеланоз. Також поширені діабетична дермопатія і синдром діабетичної стопи з виявами порушення пігментації, зокрема чорним акантозом і вітиліго.

Відмінності між типами ураження залишаються неясними для різних типів ЦД (типу 1 або типу 2). Загалом шкірна інфекція і ксероз виявилися дуже поширеними і важливими шкірними захворюваннями в кількох дослідженнях, незалежно від типу ЦД. Шкірні інфекції грибкової етіології є найбільш поширеними, а інфекції бактеріального походження трапляються рідше.

ЦД впливає на шкіру за допомогою кількох механізмів. Високий рівень глікемії дуже впливає на гомеостаз шкіри, порушуючи нормальне функціонування кератиноцитів *in vitro*, зменшуючи їхню проліферацію і диференціювання. Вони також призводять до утворення кінцевих продуктів глікування (КПГ). Останні утворюються внаслідок глікування білків, ліпідів і нуклеїнових кислот. Вони мають різні патологічні впливи на шкіру: утворюють активні форми кисню (АФК), погіршують кліренс АФК та функцію внутрішніх позаклітинних білків, індукують прозапальні цитокіни за допомогою шляху ядерного фактора κβ (NF-κβ). КПГ змінюють властивості колагену, зменшуючи його гнучкість і розчинність та збільшуючи жорсткість, потовщуючи шкірний колаген, збільшуючи зшивання за рахунок неферментативного глікування, та беручи участь у розвитку фіброзу. У пацієнтів з цукровим діабетом судинні зміни в шкірі аналогічні змінам, спричиненим впливом ультрафіолету, зокрема потовщення стінок судин, яке збільшується від стегна до стопи і найбільш виражене в капілярах, що призводить до порушення чутливості судин.

Ця стаття має на меті узагальнення всіх цих патологій, надання інформації щодо їхньої поширеності, короткий опис симптомів, патогенезу і принципів їхнього лікування. Дерматологи відіграють ключову роль у їхньому лікуванні, а також у виявленні нових випадків ЦД. Вони також повинні контролювати глікемію у цих пацієнтів.

Ключові слова: цукровий діабет, поширеність, шкірні інфекції, діабетична дермопатія, діабетична стопа.

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Кожные расстройства у пациентов с сахарным диабетом: обзор литературы

Сахарный диабет (СД) — это частое метаболическое заболевание, распространенность которого оценивается примерно в 9,3 % среди населения мира в возрастной группе 20—79 лет, что соответствует 463 млн больных. Более того, заболеваемость этой болезнью, вероятно, увеличится в течение последующих лет. На его долю приходится более 90 % больных сахарным диабетом. Системные осложнения также могут наблюдаться в дерматологии. В зависимости от региона распространенность кожных заболеваний у больных СД составляет от 35,4 до 98,8 %, что делает эти симптомы частым поводом для консультаций в дерматологической практике. Наиболее распространенными заболеваниями являются кожные инфекции, но также часто могут наблюдаться желтые ногти, кандидоз, акрохордоны, ограниченная подвижность суставов и идиопатический каплевидный гипомеланоз. Также распространены диабетическая дермопатия и синдром диабетической стопы с проявлениями нарушения пигментации, в частности черным акантозом и витилиго.

Различия между типами поражения остаются неясными для различных типов СД (типа 1 или типа 2). В целом кожная инфекция и ксероз оказались очень распространенными и важными кожными заболеваниями в нескольких исследованиях, независимо от типа СД. Кожные инфекции грибковой этиологии являются наиболее распространенными, а инфекции бактериального происхождения встречаются реже.

СД влияет на кожу с помощью нескольких механизмов. Высокий уровень гликемии сильно влияет на гомеостаз кожи, нарушая нормальное функционирование кератиноцитов *in vitro,* уменьшая их пролиферацию и дифференцировку. Они также приводят к образованию конечных продуктов гликозилирования (КПГ). Последние образуются в результате гликолизирования белков, липидов и нуклеиновых кислот. Они имеют различные патологические воздействия на кожу: образуют активные формы кислорода (АФК), ухудшают клиренс АФК и функцию внутренних внеклеточных белков, индуцируют провоспалительные цитокины с помощью пути ядерного фактора κβ (NF-κβ). КПГ изменяет свойства коллагена, уменьшая его гибкость и растворимость и увеличивая жесткость, утолщая кожный коллаген, увеличивая сшивание за счет неферментативного гликозилирования, и участвуя в развитии фиброза. У пациентов с сахарным диабетом сосудистые изменения в коже аналогичны изменениям, вызванным воздействием ультрафиолета, в частности утолщение стенок сосудов, которое увеличивается от бедра до стопы и наиболее выражено в капиллярах, что приводит к нарушению чувствительности сосудов.

Эта статья имеет целью обобщение всех этих патологий, предоставление информации по их распространенности, краткое описание симптомов, патогенеза и принципов их лечения. Дерматологи играют ключевую роль в их лечении, а также выявлении новых случаев СД. Они также должны контролировать гликемию у этих пациентов.

Ключевые слова: сахарный диабет, распространенность, кожные инфекции, диабетическая дермопатия, диабетическая стопа.

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