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Cutaneous complications in diabetes mellitus: pathophysiology, clinical relevance and the role of physical activity in prevention – a literature review

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Abstract

Introduction and Purpose:

Diabetes mellitus is a chronic metabolic disease leading to a number of complications, including skin lesions, which may be the first sign of hyperglycaemia or indicative of advanced disease. In recent years, increasing attention has been paid to the role of physical activity not only in improving glycaemic control, but also in reducing the pathophysiological processes responsible for the cutaneous manifestations of diabetes. The aim of this study was to present the most common cutaneous lesions in patients with diabetes, their mechanisms of formation and to assess the impact of physical activity on their occurrence and course.

Methods:

Literature from the PubMed and Scopus databases was analysed, focusing on publications on the associations between skin lesions in diabetic patients and levels of glycaemic control, oxidative stress, vascular disorders and the impact of regular physical activity.

Conclusions:

Cutaneous manifestations of diabetes, such as dermopathy, infections, lichen sclerosus or acanthosis nigricans, are associated with chronic hyperglycaemia, microangiopathy and neuropathy. Physical activity improves microcirculation, reduces inflammation and AGE accumulation, which can alleviate skin lesions. Therefore, dermatological assessment should be a regular part of diabetes care and regular adapted physical exercise an important support of metabolic and dermatological therapy.

Key words: diabetes mellitus; skin manifestations; cutaneous complications; physical activity

1. Introduction

Diabetes mellitus is a complex metabolic disease that affects body function in a systemic way, involving not only glucose metabolism, but also the cardiovascular, nervous, immune and skin systems. The skin, as an organ available for clinical examination, plays a special role in the diagnosis and monitoring of the course of the disease. Skin manifestations - both specific, such as acanthosis nigricans, diabetic dermopathy or necrobiosis lipoidica, and non-specific,

such as dryness, pruritus or infections - can be indicators of unbalanced glycaemia, insulin resistance and microangiopathic and neuropathic complications [1,2].

In recent years, there has been increasing emphasis on the role of non-pharmacological treatments for diabetes, including physical activity [3]. In addition to improving glycaemia and reducing insulin resistance, physical exercise modifies processes such as oxidative stress, chronic inflammation, protein glycation and microcirculatory disturbances - key mechanisms responsible for the development of skin lesions. Furthermore, moderate physical activity promotes wound healing, improves skin perfusion and reduces the risk of complications such as foot ulcers [4].

The aim of this review paper is to discuss the clinical cutaneous manifestations of diabetes in relation to its pathophysiology and to outline the potential role of physical activity as a factor supporting the prevention and treatment of dermatological complications of the disease.

2. Epidemiology of skin lesions in diabetes mellitus

Cutaneous manifestations are a common comorbidity in diabetes, with their occurrence and characteristics depending on the type of the condition, its duration and the level of metabolic control. Studies show a higher rate of dermatoses in patients with type 2 diabetes (up to 71%) compared to those with type 1 diabetes (about 51%), which may be related to more frequent insulin resistance and longer duration of undiagnosed hyperglycaemia [5]

The degree of glycemic control, as assessed by glycated hemoglobin (HbA1c) values, has a significant impact on the frequency and severity of dermatological lesions. Clinical studies indicate that higher HbA1c values correlate with a higher number and more severe course of skin lesions, especially such as diabetic dermopathy, skin infections and lichen sclerosus [1].

Another important epidemiological factor is the duration of the disease. A study conducted on 300 patients, found that as many as 78% of people with diabetes showed skin lesions, with their frequency and variation increasing significantly in patients with disease duration of more than 10 years. Fungal infections, diabetic dermopathy, dry skin (xerosis) and lichen planus were the most common, the presence of which showed an association with chronically elevated blood glucose levels [6].

The long-term course of diabetes also predisposes to the development of complications such as neuropathy and angiopathy, which lead to trophic disorders of the skin and increase its susceptibility to infectious agents [7].

3. Pathophysiology of skin lesions in diabetes

Chronic hyperglycaemia in diabetes induces glucotoxicity, oxidative stress, and activation of harmful metabolic pathways, damaging cells and impairing endothelial function. It weakens immunity and disrupts wound healing due to neutrophil, macrophage, and fibroblast dysfunction [8,9]. Glucotoxicity and oxidative stress activate the polyol and hexosamine pathways, increasing ROS production, which damages tissues and promotes inflammation, insulin resistance, and vascular complications [10]. In diabetes, immune system dysfunction promotes chronic inflammation, delayed wound healing and impaired angiogenesis [11]. Dysregulated fibroblast function and microRNA-26a expression further worsen tissue repair [12]. Advanced glycation end-products (AGEs) stiffen collagen fibers, reducing skin elasticity and healing capacity. Glycation also disrupts collagen metabolism, accelerating skin aging and vulnerability to injury [13,14]. Peripheral neuropathy leads to impaired sensation, which increases the risk of unnoticed injuries, ulcers and infections. These changes collectively lead to chronic wounds and foot complications, requiring preventive care and multidisciplinary management [15,16].

4. Reversing pathophysiological mechanisms through physical activity

Regular physical activity contributes to the inhibition of key pathophysiological processes induced by chronic hyperglycaemia, such as oxidative stress, inflammation, insulin resistance and accumulation of AGEs.

4.1. Improving tissue insulin sensitivity

Physical activity potentiates the sensitivity of peripheral tissues, especially striated muscles, to insulin. Glucose utilisation in muscle cells is improved, leading to lower glycaemia and reduced insulin resistance. Endurance training has been shown to reduce oxidative stress in muscle and to have a beneficial effect on the cytokine profile, independent of weight reduction [17].

4.2. Reduction in levels of pro-inflammatory cytokines (e.g. TNF-α, IL-6)

Physical activity reduces pro-inflammatory cytokines such as TNF-α and IL-6, which contributes to improved carbohydrate and lipid metabolism and reduced risk of vascular complications. In intervention studies, regular exercise has been shown to reduce inflammation in adipose tissue in older people, which may have important metabolic implications [18].

4.3. Reducing oxidative stress

Physical training increases the activity of antioxidant enzymes and improves mitochondrial function, leading to reduced production of reactive oxygen species (ROS) and reduced cellular damage. The result is more effective protection of cells against the damaging effects of reactive oxygen species [19].

4.4. Improving cutaneous microcirculation

Dysfunction of the cutaneous microcirculation is a common complication of diabetes, contributing to delayed wound healing and an increased risk of ulcers, especially in the feet. Even a single bout of physical exercise can improve skin tissue perfusion in diabetics, which may contribute to accelerated healing and reduced incidence of skin complications [20].

4.5. Reducing the accumulation of advanced glycation products (AGEs)

AGEs play a key role in the development of chronic complications of diabetes, such as skin, vascular and nerve damage. Regular physical activity, by improving glycaemic control and reducing oxidative stress, can limit their accumulation, thereby reducing the risk of micro- and macrovascular complications and skin lesions [21].

5. Skin manifestations accompanying diabetes mellitus - classification and characteristics

5.1. Lesions specific to diabetes mellitus

Among the skin lesions associated with diabetes mellitus, there are several characteristic clinical entities whose incidence and clinical picture may be important indicators of metabolic disorders accompanying the disease.

Acanthosis nigricans (AN) is a cutaneous manifestation of insulin resistance, characterized by the presence of dark, velvety patches located most often within skin folds, such as the neck, armpits and groin area. In a study of 311 patients with type 2 diabetes, AN was found to be present in 52.7% of participants, with the presence of skin lesions significantly correlating with higher body mass index (BMI), particularly ≥ 25 kg/m^2 [22]

Importantly, other studies have shown that AN can also occur in normal-weight individuals and its presence is positively correlated with elevated fasting insulin levels and HOMA-IR. These observations suggest that AN may serve as an early and readily available clinical indicator of the risk of developing type 2 diabetes and the metabolic syndrome, especially in populations with a high prevalence of insulin resistance and obesity [23].

Diabetic dermopathy (DD) is one of the most common skin lesions in diabetic patients, characterized by the presence of atrophy and hyperpigmented atrophic patches, mainly on the

anterior surface of the shin. The presence of diabetic dermopathy is often correlated with the presence of other microangiopathic complications, such as nephropathy, retinopathy or polyneuropathy, making it an important diagnostic indicator suggesting advanced vascular changes in diabetic patients [24].

Necrobiosis lipoidica (NL) is a rare chronic inflammatory dermatosis that occurs in about 0.3% of patients with diabetes. The skin lesions are most often localized on the anterior surface of the shin, taking the form of yellowish-brown, infiltrative patches with an atrophic center and purple edges [25].

Scleredema diabeticorum (SD) is a low-prevalence skin manifestation characterized by thickening of the skin, most commonly in the neck and upper back. In an analysis involving 484 people diagnosed with diabetes, symptoms of scleredema diabeticorum were reported in 2.5% of patients, with the phenomenon more frequently observed among type 2 diabetics [26].

5.2. Non-specific lesions, more common in people with diabetes

Bacterial infections

Studies have documented that skin and soft tissue infections (SSTIs) are significantly more frequent and severe in people with diabetes compared to the general population. The most commonly identified pathogen in these infections was Staphylococcus aureus, including methicillin-resistant strains (MRSA), responsible for a large proportion of cases of abscesses, boils and folliculitis. Patients with diabetes also have a higher risk of complications, such as the need for hospitalization, re-treatment or progression of infection, which may be due to a weakened immune response and hyperglycaemia that promotes microbial growth [27].

Fungal infections

People with diabetes mellitus have an increased incidence of fungal infections of various locations, due in part to impaired immunity and favorable metabolic conditions for microbial growth. The most commonly isolated pathogens are fungi of the Candida and Aspergillus genera, found in skin lesions, on mucous membranes and in deeper tissues. Unbalanced glycemia further complicates treatment and promotes the chronic course of these infections, requiring special clinical vigilance [28,29].

Pruritus of the skin

Pruritus in patients with type 2 diabetes is a common symptom, often associated with peripheral neuropathy and microcirculatory disorders. A study published in 2021 found that pruritus occurs in diabetic patients at a rate of 18.4% to 27.5%. The most commonly reported locations of the condition included the lower extremities, feet and lumbar region, which may suggest an association with the presence of peripheral neuropathy and microcirculatory disorders in these body regions [30].

Dry skin (xerosis)

Dry skin is one of the most common dermatological complications observed in patients with diabetes, especially in the lower extremities. Disorders of the skin's water-lipid balance in the course of hyperglycaemia lead to excessive dryness of the skin, which promotes the formation of cracks, erosions and increases the risk of secondary infections and ulcerations [31].

6. Chronic complications with cutaneous manifestation

Diabetic foot

Diabetic foot syndrome (DFU) is a serious complication of chronic, poorly controlled diabetes, most often manifested by the presence of ulcers on the sole surface of the foot. It is estimated that this problem affects about 15% of patients with diabetes, of which 14-24% of cases lead to the need for amputation, usually as a result of infections of deep structures such as bones. The co-occurrence of peripheral neuropathy, lower extremity ischemia and infection plays a key role in the pathogenesis of DFU, creating a characteristic triad of risk factors [32].

Joint stiffness syndrome (cheiroarthropathy)

Joint stiffness syndrome in people with diabetes is manifested by progressive restriction of range of motion, mainly in the small joints of the hands, leading to difficulty in straightening the fingers. Painless stiffening of the joints (often bilateral) is characteristic, which can impair fine manual activities and reduce patients' quality of life [33].

Trophic changes in nails and hair

A study published in 2017 assessed the condition of hair follicles and nail plates in patients with diabetes, focusing on the cutaneous manifestations of peripheral neuropathy. The analysis included 100 patients with type 2 diabetes, 68% of whom showed changes in the hair follicles, such as atrophy or reduced numbers, suggesting a disruption in the hair growth cycle associated with neuropathy. In addition, 54% of patients presented nail plate abnormalities, including thickening, transverse furrowing and changes in shape, which may indicate chronic microvascular disorders and peripheral neuropathy. These findings underscore the importance

of regular monitoring of skin lesions in patients with diabetes, which may be early indicators of the development of peripheral neuropathy [34].

Lipohypertrophy

Lipohypertrophy is the pathological thickening of adipose tissue at the site of repeated insulin injections, a common complication of type 2 diabetes treatment that can lead to impaired insulin absorption and worsened glycemic control. A multicenter study conducted in southern Italy found that lipohypertrophy occurs in 37.3% of insulin-treated patients with type 2 diabetes. Key risk factors include failure to change injection sites, repeated use of the same needle and long-term insulin therapy [35].

7. Skin as a clinical indicator of metabolic disorders and diabetes complications

Skin lesions are an important, though often underestimated, part of the clinical picture of metabolic disorders, including insulin resistance and type 2 diabetes mellitus. Selected dermatoses, such as acanthosis nigricans, diabetic dermopathy, necrobiosis lipoidica or recurrent skin infections, can act as early and readily available indicators of a developing metabolic disease. In addition, their presence may reflect the effectiveness of ongoing therapy and indicate the presence of organ complications.

7.1.Skin lesions as an early marker of metabolic disorders

Acanthosis nigricans, especially common in obese children and adolescents, is closely associated with hyperinsulinemia and considered one of the first signs of insulin resistance. As a visible and easily recognizable skin lesion, it can be an important clinical signal prompting the evaluation of metabolic parameters, even before the onset of overt glycemic disturbances. Early recognition of this symptom makes it possible to implement preventive measures and delay progression to type 2 diabetes [23,36].

Recurrent and difficult-to-treat skin infections, such as boils and ringworm, are a common problem in patients with impaired glucose homeostasis [9,11].

Chronic hyperglycemia impairs the immune response through neutrophil dysfunction and persistent inflammation, which increases the risk of infections. Their presence should prompt screening for diabetes, as they may represent its first clinical manifestation [37,38].

7.2. Dermatologic manifestations as a reflection of metabolic control

In patients diagnosed with diabetes, skin manifestations can be a useful tool in assessing metabolic compensation. Lesions such as acanthosis nigricans, fungal infections, diabetic

dermopathy or trophic nail plate disorders show a correlation with higher glycated hemoglobin values [39]

In observational studies in patients with diabetic dermopathy, mean HbA1c levels exceeded 9%, indicating a significant association between the severity of skin lesions and uncompensated glycemia [40,41].

Importantly, improvements in metabolic control can lead to gradual resolution of some dermatological lesions, further confirming their usefulness as non-invasive indicators of treatment efficacy. Regular assessment of skin condition should be part of routine monitoring of patients with diabetes, supporting early detection of complications and increasing the effectiveness of therapeutic interventions [39].

7.3. Skin as an indicator of organ complications in diabetes

Dermatologic manifestations of diabetes can also indicate the presence of chronic organ complications, particularly microangiopathy. Diabetic dermopathy has a documented correlation with retinopathy and nephropathy, and skin lesions not infrequently precede the clinical manifestation of vascular complications [42].

The presence of ulceration, necrosis, chronic fungal infections or trophic changes may suggest advanced peripheral neuropathy, immunosuppression or diabetic nephropathy [40,41].

In addition, some dermatoses, such as acanthosis nigricans or necrobiosis lipoidica, may act as early signals of comorbid metabolic disorders, dyslipidemia or insulin resistance, justifying the need for expanded diagnostics for systemic complications [31].

7.4. Importance of early recognition and interdisciplinary collaboration

Incorporating skin manifestations into the diagnostic process and monitoring of patients with metabolic disorders requires raising the level of clinical awareness among both dermatologists and primary care physicians. Training and the incorporation of diagnostic tools in daily practice can significantly improve the detection of diabetes and its complications, leading to faster therapeutic intervention. The skin, as a readily accessible organ, provides valuable clinical information and should be systematically evaluated as part of comprehensive diabetes care [36].

8. Adapting physical activity to dermatological complications

Despite the numerous health benefits, the presence of skin complications in diabetes can be a barrier to undertaking regular physical activity. Lesions such as diabetic neuropathy, diabetic

dermopathy, skin infections or lipodystrophies at the site of insulin injection require special care.

8.1. Neuropathy and risk of skin damage

Peripheral neuropathy, a common complication of diabetes, significantly increases the risk of skin damage, especially in the feet. The loss of pain and temperature sensation leads to unnoticed injuries which, combined with microcirculatory disturbances, promote ulcer formation and delayed wound healing. As research indicates, regular risk assessment and a comprehensive foot examination are crucial for early detection of lesions and prevention of diabetic foot syndrome. In this context, exercise should be modified accordingly - forms of activity that carry a risk of foot injury, such as running on hard surfaces, should be avoided in favour of low-mechanical impact exercise, such as stationary cycling or swimming, while monitoring skin condition and using appropriate protective footwear [43].

8.2. Skin infections and mycoses

In patients with diabetes mellitus, the presence of fungal skin infections, particularly in the feet, presents a significant clinical challenge, requiring adjustments to physical activity to limit further skin damage and lesion progression. As indicated in the study, the humid and warm environment, typical of enclosed sports footwear, favours the proliferation of dermatophytes and candida, which can lead to exacerbation of the infection. It is therefore recommended to choose forms of activity that do not require the wearing of sealed footwear for long periods of time, and to implement appropriate hygiene procedures before and after exercise [44].

8.3. Lipodystrophies and physical activity

Insulin lipodystrophies, such as lipohypertrophy, are a common complication in diabetic patients using multiple insulin injections. These lesions can cause discomfort during physical activity, affecting the efficiency of insulin absorption and increasing the risk of mechanical injury at injection sites. Therefore, it is important to avoid injecting into muscles actively involved in exercise when planning physical activity and to use rotation of insulin injection sites, which minimises the risk of skin complications and promotes the patient's metabolic stability [45].

8.4. Diabetic dermatopathy and other dermatoses:

Diabetic dermopathy, characterised by brown, scaly patches on the skin of the legs, is one of the most common dermatological complications in patients with diabetes. These lesions are

the result of damage to the small blood vessels and can lead to impaired blood supply to the skin, increasing the risk of infection and ulceration. Regular physical activity improves skin microcirculation, which can help reduce the risk of skin complications associated with diabetes. However, if diabetic dermopathy is present, intense pressure on the affected areas of the skin should be avoided to prevent damage during physical activity. The use of appropriate footwear and avoidance of activities that may lead to skin trauma to the affected areas is recommended

9. Importance of individualised skin care in patients with diabetes

Individualised skin care is an essential part of the holistic management of the patient with diabetes, aiming not only to improve comfort but also to prevent skin and systemic complications. Studies show that daily application of appropriate preparations, such as emollients or urea-containing creams, can improve skin barrier function, reduce dryness and itching, resulting in a better quality of life for diabetic patients [46].

In addition, appropriately selected skin care can reduce the risk of developing skin lesions secondary to chronic hyperglycaemia, such as neuropathy or microangiopathy. Importantly, an individualised approach is also applicable to the treatment of skin complications such as foot ulcers or recurrent fungal and bacterial infections. Proper hygiene, regular skin inspection and the use of specialised treatment and care products accelerate wound healing and reduce the risk of progression to more serious conditions requiring hospitalisation [31].

In the context of medical staff education, it is essential that primary care physicians are aware of the role of daily skin care and have the tools and knowledge to implement strategies individually tailored to the patient's needs.

Conclusions

The skin, being a ‘mirror’ of the body's metabolic state, plays an important role in the clinical imaging of diabetes. Dermatological manifestations may provide the first warning of glycaemic disturbances, as well as reflecting the degree of disease compensation and the presence of complications. Assessment of skin lesions should be an integral part of the clinical examination of the diabetic patient - both at the diagnostic stage and when monitoring the effectiveness of therapy.

Physical activity, by beneficially modifying metabolic and vascular processes and suppressing chronic inflammation, can have a beneficial effect on the course of dermatological complications of diabetes. Improving microcirculation, reducing oxidative stress and reducing

the formation of AGEs are just some of the mechanisms through which exercise can have a protective effect on the skin. However, if dermatological changes such as infections, ulcers or neuropathy are present, it is advisable to individualise training recommendations.
Incorporating regular exercise into a comprehensive diabetes therapeutic plan can not only improve overall metabolic status, but also promote skin health and reduce the risk of dermatological complications. An integrated therapeutic approach, incorporating elements of diabetology, dermatology and physiotherapy, should form the basis of comprehensive diabetes care, particularly in the context of co-occurring skin complications and functional limitations.

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Methodology: PSK, AEF, PMD;
Software: PMD, TKK;
Check: PSK, AS, MB;
Formal analysis: KK, ND;
Investigation: MS, AS, WK, PMD;
Resources: AEF, MB, TKK;
Data curation: KK, AEF, PMD, TKK, AS, MB, ND, MS, WK, PSK;
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