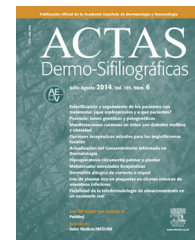




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## REVIEW

# Cutaneous Manifestations in Children with Diabetes Mellitus and Obesity<sup>☆</sup>



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Revisión

**Abstract** Obesity and diabetes are chronic diseases that affect people all over the world, and their incidence is increasing in both children and adults. Clinically, they affect a number of organs, including the skin. The cutaneous manifestations caused or aggravated by obesity and diabetes are varied and usually bear some relation to the time that has elapsed since the onset of the disease. They include soft fibromas, acanthosis nigricans, striae, xerosis, keratosis pilaris, plantar hyperkeratosis, fungal and bacterial skin infections, granuloma annulare, necrobiosis lipoidica, psoriasis, and atopic dermatitis.

In this review article we present the skin changes found in children with diabetes mellitus and obesity and related syndromes and highlight the importance of the skin as a tool for establishing clinical suspicion and early diagnosis of systemic disease.

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### Manifestaciones cutáneas en niños con diabetes mellitus y obesidad

**Resumen** La obesidad y la diabetes son 2 enfermedades crónicas de distribución mundial, de incidencia en aumento tanto en niños como en adultos. Clínicamente se caracteriza por comprometer distintos órganos, entre ellos la piel. Las manifestaciones cutáneas secundarias o agravadas por la obesidad y la diabetes son variadas, y en su mayoría están relacionadas con el tiempo de evolución. Entre ellas se incluyen: fibromas laxos, acantosis nigricans, estrías, xerosis, queratosis pilar, hiperqueratosis plantar, infecciones cutáneas por hongos y bacterias, granuloma anular, necrobiosis lipoidea, psoriasis y dermatitis atópica, entre otros.

En esta revisión presentamos los hallazgos cutáneos en niños con estas 2 enfermedades; como también en los síndromes relacionados, recordando la importancia de la piel como herramienta para la sospecha clínica y el diagnóstico temprano de enfermedades sistémicas.

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## Introduction

Obesity and diabetes are 2 chronic diseases with worldwide distribution that affect several organs, including the skin.<sup>1</sup> Although both diseases are more common in adults, their prevalence in the pediatric population is growing. According to the World Health Organization, 20% of children and adolescents in Europe are overweight and, of these, a third are obese.<sup>2</sup> Currently, 3700 cases of noninsulin-dependent diabetes are diagnosed annually in children and adolescents,<sup>3</sup> a figure clearly higher than that previously reported.<sup>4</sup> Given the current situation, physicians can expect to encounter a growing number of patients with clinical conditions related to these diseases.

The cutaneous manifestations of diabetes and obesity are directly related to the age of onset, duration, and severity of the underlying disease. This review article is divided into 2 sections based on existing classification schemes: the first deals with the cutaneous manifestation associated with diabetes, and the second with those associated with obesity.

## Diabetes

Diabetes mellitus is a heterogeneous group of disorders characterized by elevated blood sugar and impaired lipid and carbohydrate metabolism.<sup>5</sup> It is classified according to pathogenesis as type 1 (DM1) or type 2 (DM2), and each type has specific clinical characteristics. DM1 is the result of the destruction, probably by way of an autoimmune process, of insulin-producing B-cells in the pancreatic islets. It is characterized by abrupt onset, insulin deficiency, a tendency to progress to ketoacidosis even in the early stages, and absolute dependence on exogenous insulin to sustain life. In the case of DM2, patients may be relatively asymptomatic for many years and have a twofold defect: deficient insulin action (insulin resistance) and deterioration of B-cell function. These patients may have low, normal, or elevated insulin levels. The typical patient with DM2 is an obese person with a family history of diabetes.

The complications associated with diabetes are multifactorial in origin, occurring as a result of biochemical, structural, and functional abnormalities.<sup>6</sup> Of particular note among the anomalies found in diabetic patients is the acceleration of the biochemical process of advanced glycation as a result of chronic hyperglycemia and increased oxidative stress. Advanced glycation involves the generation of a diverse group of chemical substances known as advanced glycation end products (AGEs), which react with specific receptors to produce adverse effects.<sup>7</sup> The production of AGEs is secondary to a nonenzymatic reaction of glucose with proteins, lipids, and nucleic acids.

Some 30% of adult diabetic patients will present cutaneous manifestations at some time in their lives; the timing will vary depending on the type of diabetes and the patient's age at onset. Children are no exception. DM1 is the most common type of diabetes in children,<sup>4</sup> with a mean age at onset of 8 years. It can be associated with growth disorders and autoimmune diseases as

well as manifestations related to microvascular changes. Owing to the increasing prevalence of obesity and insulin resistance in children, the prevalence of DM2 has also increased in the younger population, particularly among adolescents.<sup>3</sup>

Since there are very few review articles on the classification of the cutaneous manifestations of diabetes in either children or adults, we have classified them using the schema proposed in 1985 by Edidin,<sup>4</sup> which differentiates between skin disorders secondary to diabetes, skin disorders that occur more frequently in diabetic patients, cutaneous manifestations of insulin resistance, and skin disorders associated with insulin therapy (Table 1).

## Skin Disorders Secondary to Diabetes

High blood sugar levels and the damage to vascular and nerve structures characteristic of diabetes produce cutaneous manifestations such as xerosis, faciei rubeosis, limited joint mobility, infections, microangiopathy, and neuropathy.

### Xerosis and Thickening of the Skin

Xerosis, or dry skin, is one of the earliest and most common signs of diabetes and is found in up to 22% of patients with DM1.<sup>8</sup> Xerosis has been demonstrated by measuring transepidermal water loss and the high-frequency conductance of the forearm.<sup>9</sup> Another finding of interest is that even in the absence of clinically evident xerosis, the skin of patients with diabetes exhibits abnormal desquamation and reduced elasticity<sup>10</sup> as well as a greater than average thickness that may contribute to a reduction in elasticity.<sup>11</sup> Skin thickening is classified clinically into 3 categories: a) benign thickening of the skin; b) scleroderma-like syndrome; and c) scleredema of Buschke. It is thought that skin thickening in this setting is caused by abnormal collagen glycation during episodes of hyperglycemia or by collagen proliferation promoted by excess insulin.<sup>12</sup> The hands and feet are the most common sites of benign skin thickening in diabetic patients, and involvement of these sites is closely associated with joint limitation.<sup>13</sup> Although the condition may be asymptomatic, increased skin thickness can be measured using cutaneous ultrasound.<sup>11</sup>

### Keratosis Pilaris

Keratosis pilaris is a common condition in diabetic children, with a prevalence of 11.7% in patients with DM1 over 10 years of age.<sup>8</sup> The etiology is unclear, but it appears that xerosis plays an important role.<sup>14</sup> The clinical characteristics include rough follicular papules and variable erythema located predominantly on the extensor surfaces of the arms and legs and occasionally on the face, buttocks, and trunk (Fig. 1). Keratosis pilaris tends to flare up in winter and usually improves during the summer months.<sup>15</sup> It is mainly associated with atopic dermatitis and an high body mass index.<sup>16</sup> Treatment includes keratolytic agents, retinoids, and low potency topical corticosteroids.<sup>17</sup>

### Rubeosis Faciei

Rubeosis faciei diabetorum—the characteristic facial rash found in diabetic patients (Fig. 2)—is caused by the dilation

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