

## Research Article

## The Frequency of Dermatological Diseases in Insulin Dependent Diabetic Sudanese Children

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**Abstract:** Diabetes mellitus type I (IDDM) is growing up health problem among Sudanese young population. A lot of dermatological diseases are known to occur in diabetic patients may be due to odd metabolism or as a complication of the disease. The aim of the study is to assess the frequency of skin manifestations in children with type I diabetes mellitus.

The study recruited 151 IDDM children matched for age with 76 normal children as a control group. Dermatological and general clinical examinations were undertaken for two groups in addition to retinal examination and HbA1c level measurement in the IDDM patients. Patients were seen at Albolok diabetic clinic; heights and weights were measured, age of onset, control and medical history were taken by filling a well formed questionnaire. Xerosis was seen in 35% of IDDM patients ( $p < 0.000004$ ) and 2% of control group. There were 6% of patients developed diabetic hand changes and 5% had retinal changes. The lipohypertrophy, lipoatrophy and hyper pigmentation had high frequencies, 22%, 13%, and 47% respectively. Eczema had seen in 10% of patients while atopic dermatitis was seen in 2% and seborrhic dermatitis in 6.6%. Gluten enteropathy and viral warts detected in 2% of patients. Impetigo as folliculitis was seen on 1.3% of cases. The current study showed the high prevalence of xerosis in IDDM that may appear the first changes take place in young IDDM patients and its association with diabetic hands and retinal changes. The relative high frequency of dermatitis may raise the importance of the altered immunological responses in this group. The large group prospective study will help a lot to detect complications in young patients and prospect them in elder ones.

**Keywords:** Diabetes mellitus type I, Xerosis, lipohypertrophy, lipoatrophy.

### INTRODUCTION

Diabetes mellitus (DM) is a worldwide problem and it is estimated that the number of diabetic patients will grow from 135 million to 300 million by the year 2025 [1]. Affected organs include the cardiovascular, renal and nervous systems, eyes and the skin [1]. The cutaneous manifestations of DM can be classified in four categories: 1- Skin disease with strong to weak association with diabetes (Necrobiosis lipoidica, diabetic dermopathy, yellow skin, eruptive xanthomas, acanthosis nigricans, oral leukoplakia, lichen planus). 2- Infections (bacterial, viral, fungal). 3- Cutaneous manifestations of diabetic complications (microangiopathy and macroangiopathy). 4- Skin reactions to anti-diabetic treatment (insulin and sulphonylurea) [2]. The skin manifestations of diabetes are the result of multiple factors. Abnormal carbohydrate metabolism, other altered metabolic pathways, atherosclerosis, microangiopathy, neuron degeneration, and impaired host mechanisms all play a role [3]. Skin of diabetic patients has increased capillary fragility, and blood vessels show decreased circulation. Skin and soft tissue is the most common site for bacterial infections, and has been reported in up to 30% diabetics [4]. *Candida albicans* can cause angular

cheilitis, vulvovaginitis, balanitis, finger web space infection and paronychia in poorly controlled diabetics. *Necrobiosis lipoidica* is an asymptomatic disease with oval sharply demarcated reddish brown plaques occurring mostly over anterior legs. It may also manifests as solitary nodule on the hands, fingers, forearms, face and scalps [4]. Urbach showed that skin sugar levels run parallel to the blood sugar levels [5]. Cutaneous signs of diabetes mellitus are extremely valuable to the clinician as some of them can alert the physician to the diagnosis of diabetes and also reflect the status of glycemic control and lipid metabolism [6]. It has been observed that without control of diabetes, the treatment response is poor in cutaneous complications [7]. Besides cutaneous manifestations certain skin diseases are strongly associated with diabetes mellitus. Thus, the study will be done to analyze the pattern of diabetic dermatoses among type I diabetic patients, in view of increasing prevalence of diabetes either type I or type II in the general Sudanese population

### Diabetes Mellitus Type I in Sudan

The data about the exact prevalence of insulin dependent diabetes mellitus (IDDM) among Sudanese

is very little, but some studies agreed it is not a rare condition. According to the 1985 WHO revised criteria for diagnosis and classification of diabetes mellitus; Abdelaziz Elamin, et al found that the overall crude prevalence rate of IDDM in 42,981 schoolchildren (aged 7–14 yr) in Khartoum, Sudan was 0.95/1000. The study concluded that, the IDDM in childhood is not rare in Sudan and that probably a substantial number of undiagnosed cases exist [8].

A study carried by Mahdi EM et al in 448 adult diabetic patients' in 1989, revealed that 6.3% had childhood diabetes [9].

These results show that type I diabetes mellitus is not rare syndrome among Sudanese children. In my study I will examine children that were diagnosed as type I diabetes mellitus and started treatment and follow-up. The examination will concern mainly on dermatological manifestations.

## LITERATURE REVIEW

In 1968 Rahbar published the observation that patients with diabetes mellitus have oddly behaving hemoglobin. This was subsequently demonstrated to be due to non-enzymatic condensation of glucose with hemoglobin to form stable covalent adducts. Non-enzymatic glycosylation occurs with many proteins including hemoglobin, an attachment that results in changes in the physical and chemical properties [10].

Glucose in solution exists as a stable pyranose ring in equilibrium with the open chain aldehyde form. The reaction of monosaccharides with proteins consists of the covalent linkage of the double-bonded oxygen of the aldehyde function with an NH<sub>2</sub> group, either on the alpha-amino group of the N-terminal amino acid or on the epsilon-amino group of lysine. This condensation results in the formation of a Schiff base or aldimine, and is a reversible reaction. However, following the formation of the Schiff base, there is an internal reconfiguration of the molecule, the so called Amadori rearrangement, resulting in formation of a ketoamine which tends to not revert back to the Schiff base. The rate of reaction of various carbohydrates with protein correlates with the extent to which the sugar exists in the open ring (aldehyde) form [11].

Following the condensation and reconfiguration, the Amadori products undergo a series of further reactions with amino groups on other proteins to form glucose-derived intermolecular crosslinks [11]. These collagen modifications result in a color change which has been demonstrated by spectrophotometric measurement to correlate with diabetic complications [12]. One of these advanced glycosylation products, a yellow compound, 2-(2-furoyl)-4(5)-(2-furanyl)-1H-imidazole, has been identified [13]. Quantitation of another advanced glycosylation end product in the skin, the amino acid

pentosidine, has also been demonstrated to correlate with a cumulative score of diabetic complications [14].

The process of non-enzymatic glycosylation occurs to a minor extent at normal blood sugar concentrations. This gradual glycosylation of proteins may be responsible for some of the skin changes associated with aging, and this process is apparently accelerated in persons with elevated blood sugars. Most proteins evaluated seem to be involved by this reaction which results in changes in the physical and chemical properties. Glucosylation of the red cell membrane is apparently responsible for the stiffness of diabetic erythrocytes. Glucosylation of collagen results in increased stiffness and resistance to enzymatic degradation, mechanical changes of collagen which are also characteristic for aging [15]. Protein glycosylation with changes in tertiary structure and solubility of proteins could conceivably be responsible for many of the complications of this disease [15].

## MATERIALS AND METHODS

### Type of Study

Is a cross sectional hospital – based descriptive, prospective study including between March 2012 and June 2012.

### Study Group

Both male and female type I insulin dependent diabetic children and normal school students as control group.

### Area of the Study

Albolok pediatric teaching hospital located in Khartoum state, Karay locality, North of Omdurman.

### Data Collection and Investigated Variables:

One hundred and fifty one children with type 1 diabetes ( male and female subjects), with disease onset at age  $\leq 15$  years and consecutively attending the outpatient diabetes clinic at Albolok pediatric hospital over last three months period were examined. The medical history was taken about dermatological diseases and skin and mucosal surfaces were examined. General and systemic examinations were done. During the same time frame, control healthy school children in a nearby primary school also underwent dermatological, physical and systemic examinations. DM is excluded in control group children by clinical symptoms of DM (polyuria, polyphagia, polydipsia and DKA attacks). All clinically definable cutaneous lesions were recorded in both populations. Medical files were reviewed for data on diabetes duration, Hb A1C level was checked.

## RESULTS

A 227 children, 151 insulin dependent diabetic and 76 non diabetic as a control group from both gender (tab 1) with mean age 11.1 years old (Std 3.7 years) were examined for dermatological diseases that are

related or may be associated with diabetes mellitus and insulin injection(fig .1).

Hemoglobin A1c was measured to evaluate the serum glucose level during the last 4 months (mean 12.8%) and the number of DKA attacks since the diagnosis also was concerned (3.7times)as a rough clue about disease control.The mean of duration of DM since confirmed diagnosis was 4.3 years and the age of onset mean was 6.9 years old.

The means of heights and weights of IDDM patients were calculated and were 33.9 Kgs and 136.3centimeters respectively (tab 2).

The dermatological examinations showed that about 53 patients had xerosis changes ranging from mild dry skin in most cases to severe xerotic scales in one patient (fig.2). Mild xerotic changes were detected in four control subjects. Fundal ophthalmoscopic examinations showed that 8 IDDM patients started to develop mild degenerative retinal changes but, no one affected from the control group (fig 3).

Diabetic hands were seen in nine patients of IDDM patients. Four patients had tinea pedis versus five non-diabetic children developed tinea pedis. Onychomycosis was found in one diabetic patient. Three girls and two boys had tinea capitis and pityriasis versicolor, but no one of diabetic patients have tinea capitis or corporis in addition to tinea pedis and pityriasis versicolor. As pityriasis versicolor was seen in 7 patients comparing to 4 control subjects. Impetigo and folliculitis were seen in two different patients and the later also detected in one control child. Common warts are seen in three patients while no control subject was affected. The dermatological changes at sites of insulin

injections of course confined to patients group, seen in 72 patients (fig 4) as follows; 47 developed hyperpigmentation while hypertrophy and lipoatrophy were seen in 22 and 13 patients respectively. One diabetic patient showed depigmented acral vitiligo patches, which were not detected among control group.

Eczema was seen in 16 patients 2 of them had infected eczematous lesions, 10 had dry excoriated plaques and the rest had moist oozy plaques (fig.5).

In 10 IDDM patients seborrhc dermatitis was diagnosed depending on scales are distributed in the scalp and post-auricles in 8 of patients, the other two had mild scales on the eye brows and ear pinna, the diagnosis is supported by the clinical history (table 3).

Atopic dermatitis was confirmed in 3 IDDM patients, one of them had erythematous annular lesions in his two cheeks and the others diagnosis reached by history of early life onset of itchy generalized lesions that left visible excoriation marks particularly on the cheeks. Family history of atopy was positive in all three. The control group showed no case of atopic dermatitis.

Symptomatic gluten entropathy were detected in three IDDM patients, but no one developed dermatitis herpiformis. On the other hand no one of control group gave history of gluten entropathy.

By returning to fig.1 , none of IDDM patients and control group children seemed to have rubeosis, candidiasis, café-au-lait macules, halo nevi, psoriasis, alopecia areata, striae dystensae, and parpuric dermatosis.

**Table-1: Gender Distribution in IDDM and Control Groups**

		Gender		Total
		Female	Male	
subject	non diabetic	28	48	76
	Diabetic	69	82	151
Total		97	130	227

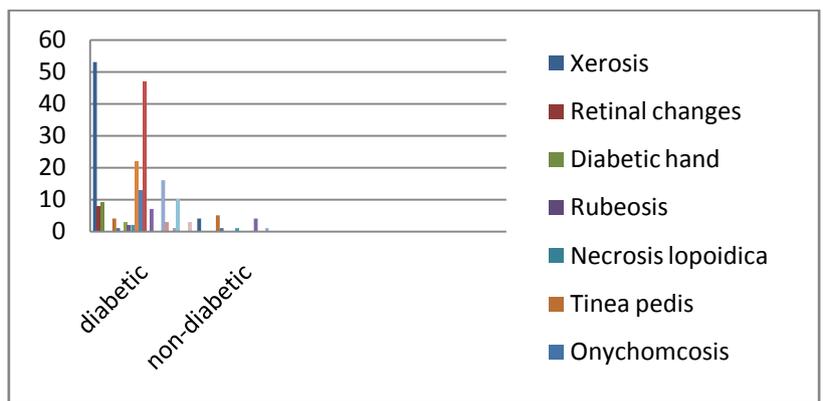
**Table-2: Age, Weight, Height, Age at Onset Duration of DM, Frequency of DKA and HbA1c in IDDM Patients and Ages of control group.**

	N	Minimum	Maximum	Mean	Std. Deviation
Height (cms)	151	4	188	136.26	25.114
Weight(kgs)	151	10	89	33.94	15.946
Age of onset of dm(years)	151	1	16	6.91	3.302
age(years)	227	3	19	11.10	3.731
Frequency of DKA	151	0	11	3.68	2.399
HbA1c(%)	151	4	26	12.84	3.938
Duration of diabetes(years)	151	1.00	13.00	4.2781	2.47698

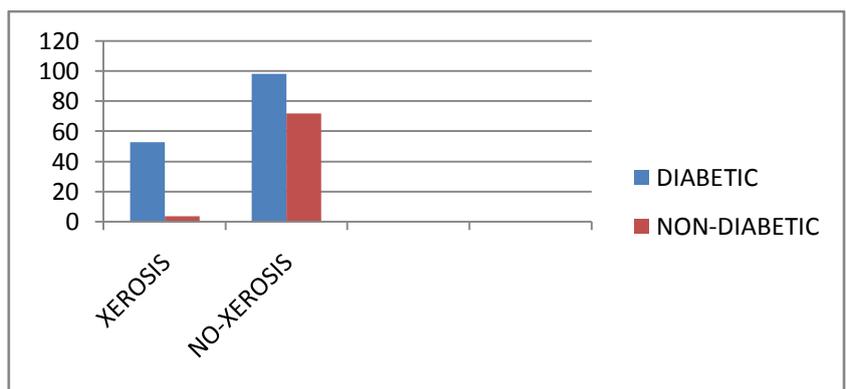
**Table-3: Seborrhic Dermatitis Prevalence in IDDM Patients and Control Group**

		SD		Total
		Absent	Present	
subject	non diabetic	76	0	76
	Diabetic	141	10	151
Total		217	10	227

P= 0.004859  
 Risk in DM patients=6.91%  
 Risk in control subjects=0.65%  
 Relative risk= 4.81%

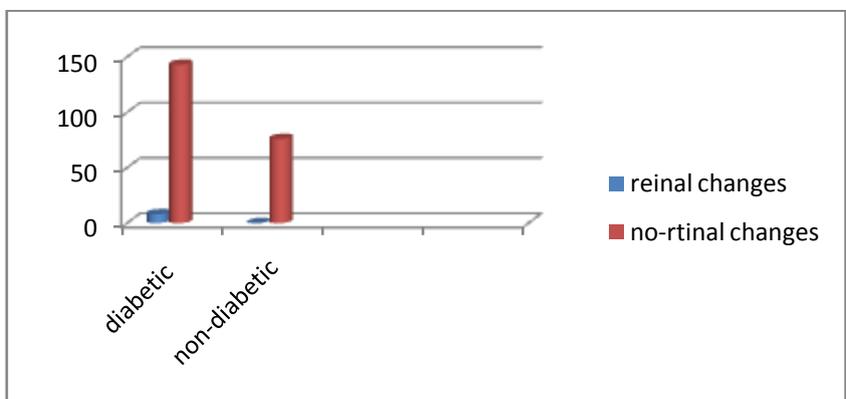


**Fig-1: Dermatological diseases in IDDM patients**



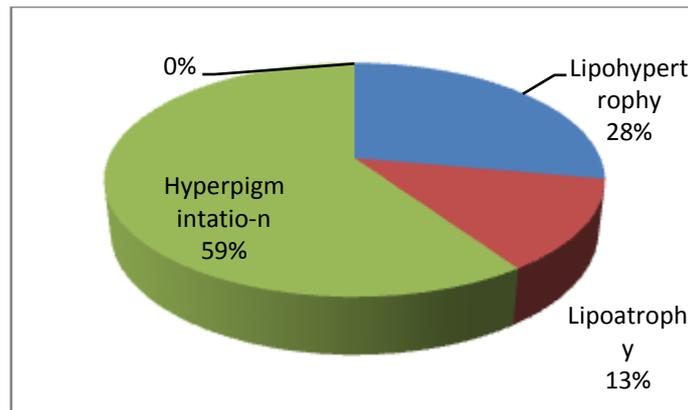
**Fig-2: Xerosis prevalence in diabetic and non-diabetic subjects**

P<0.000001  
 Risk =39.2%  
 Relative risk=26.8%

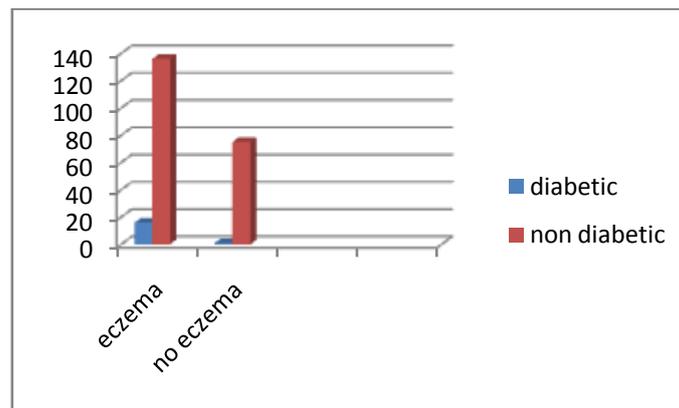


**Fig-3: Retinal changes in IDDM patients and control group**

P=0.01140  
 Risk =5.6%  
 Relative risk=3.9%



**Fig-4: Complications of insulin therapy in IDDM patients**



**Fig-5: Eczema prevalence in IDDM patients and control group**  
 P=0.004102  
 Risk in DM patients=10.60%  
 Risk in control subjects=1.32%  
 Relative risk= 7.48%

**DISCUSSION AND CONCLUSION**

The finding of greatest interest in this study is the fact that xerotic skin changes particularly of the shins, previously mentioned in the literature in association with diabetes, were found to be the most prevalent manifestation, present in various degrees of severity in almost 35% of the young diabetic patients studied. The prevalence was higher in young men than women. None of the conditions often associated with acquired ichthyosis such as nutritional deficiency, atopic skin disease, and chronic renal failure were present. Sweating disorders are considered to be common among diabetic patients, although their prevalence has not been investigated [16]. Xerosis is considered to be related to an autonomic peripheral C fiber neuropathy [17, 16]. I plan to find any relationship between the severity of xerosis and ichthyosis-like changes and the function of small C fibers by using thermal testing. It maybe speculated that other factors, such as stratum corneum adhesion and accelerated aging of the skin, may be implicated in the development of ichthyosiform skin changes in IDDM patients. There is marked correlation between xerotic skin changes on the shins and diabetic retinopathy- all patients with retinal changes have xerosis - suggests microvascular involvement in the pathogenesis of these skin changes.

Histopathological investigation is needed to further clarify this relationship. The dry palms found in 6 % of this group of patients are an additional finding that was not previously described. This finding did not reflect the presence of atopic dermatitis or contact dermatitis in my patients but was associated with scleroderma-like skin changes. The reported incidence of such changes in the literature ranges from 8 to 50% [20, 19, 18 17]. Xerotic changes were related to disease duration but not to parameters of diabetes control, similar to the findings of Seibold [19].

Diabetic shin spots, reported to be pathognomonic and among the most common skin findings in diabetic patients [21, 16], are not be found in my patients. The incidence of necrobiosis lipoidica, which is considered to be almost pathogno-monic for diabetes, was 0% in my group versus 0.6-1.2% that reported in the literature [24,23,21, 17].

The prevalence of yellow skin of the hand, rubeosis faciei, and pigmented Purpura in my study was 0% compared to that reported (21-59%) in the literature [26, 25, 17].

Regarding the prevalence of skin infections, I found that the prevalence (7%) of tinea pedis in the diabetic group is lower than the documented range according to the numbers reported by Lugo-Somolinos and Sanchez [27]. This frequency is relatively low when one considers its prevalence (6%) in the healthy control subjects. Tinea pedis was significantly associated with age, and in agreement with data reported by Lugo-Solomonis and Sanchez [27], duration of the disease and glucose control did not predict its appearance.

Of my IDDM patients, 14.5% had lipohypertrophy, 8.6% had lipoatrophy and 31% had hyperpigmentation. These reactions are considered rare [28,26,17]. However, I didn't succeed to find any epidemiological study regarding their true prevalence.

Although keratosis pilaris is considered to be a common skin disorder reportedly affecting up to 40% of the population [29], it was not present in any of the diabetic subjects, or in healthy control subjects. Several studies have shown a relationship between keratosis pilaris, skin xerosis, and atopic skin diseases [30]. Others found an association between this skin disease and obesity and hyperandrogenism [31,32].

Eczema is found in 16% and seborrheic dermatitis in 6.6% of IDDM patients with significant P values that were less than 0.005 in two diseases. Atopic dermatitis is not significantly correlated with IDDM syndrome as 1.9% but still it is somewhat high if it compared to small number of my patients and to available studies that showed low prevalence of AD among IDDM patients [33].

#### SUMMARY

This cross-sectional study has shown a high prevalence of cutaneous lesions in young IDDM patients, with the most common being ichthyosiform skin changes. Given the high prevalence of the latter and in the absence of other conditions associated with acquired ichthyosis, IDDM should be added to the list of diseases associated with this phenomenon.

Although the pathogenesis of most of the skin lesions remains unclear, a number of the skin manifestations appear to be related to other microvascular complications and to duration of diabetes.

Further studies should be performed to determine whether the detection of these skin lesions may serve as predictor markers of imminent diabetes complications, necessitating intensive follow-up and treatment.

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