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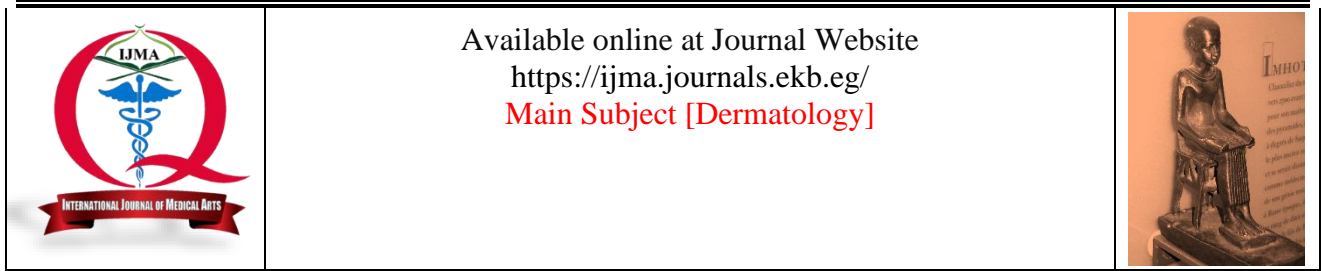
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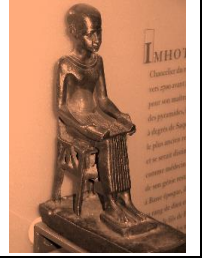
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Original Article

Prevalence of Cutaneous Disorders among Diabetic Patients in Damietta Governorate: A Cross Sectional Study

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ABSTRACT

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All authors contributed equally to this work.

Background: Long-term diabetes mellitus may disrupt skin homeostasis resulting in dermatological disorders. These manifestations may be predictors of diabetes and markers for the progression of the disease or the effectiveness of therapeutic management.

The aim of the work: This study was carried out to assess the prevalence of cutaneous disorders in diabetic patients and to determine the associations between cutaneous disorders and the patient's risk factors in the Damietta governorate.

Patients and Methods: This cross-sectional study was conducted on 947 diabetic patients. All the study participants were subjected to a questionnaire for socio-demographic characteristics, a detailed medical history, dermatological examination, and assessing body mass index [BMI] and glycated hemoglobin.

Results: Of the total of 947 diabetic patients examined for cutaneous manifestations, 595[62.8%] had one or more diabetes associated cutaneous disorders. Common cutaneous manifestations were cutaneous infections [27%], acrochordons [19.2%], pruritus [18.2%], xerosis [16.6%], acanthosis nigricans [16.2%], scleroderma-like skin changes [8.2%], and diabetic dermopathy [7.7%]. Longer duration of diabetes, poor controlled hemoglobin A1C and obesity were independent risk factors of Skin manifestations strongly associated with our studied diabetic patients.

Conclusion: As patients with diabetes have a high prevalence of cutaneous disorders, that can emerge prior to the diagnosis of diabetes and may reflect glycemic control, awareness of these manifestations will aid in the prompt and comprehensive care of both dermatoses and diabetes.

Keywords: Diabetes Mellitus; Prevalence; Cutaneous; Skin disorders.



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INTRODUCTION

Diabetes is gaining worldwide attention as a major public health problem because its prevalence affects almost every region of the world, affecting all ages and demographic subgroups as well as people of all socioeconomic backgrounds. In 2019, the global burden of diabetes is estimated at 420 million, affecting 9% of men and 8% of women [1]. Diabetes mellitus can induce alterations in a variety of organ systems. Dermatologic disorders of diabetes mellitus have a wide range of health consequences, ranging from cosmetically concerning to potentially life-threatening. Knowledge and awareness of these cutaneous disorders could provide insight into the patient's current or past metabolic status. Identifying these findings can serve as a marker for diabetes diagnosis and blood glucose monitoring [2]. The predominance of dermatological disorders among type I and Type II diabetic patients seems to be similar, but patients with type II diabetes are more likely to develop cutaneous infections, most of which are fungal, whereas patients with type I diabetes are more likely to develop autoimmune-type cutaneous lesions [3]. According to several studies, 30-82 percent of diabetic patients develop various forms of dermatological disorders during the chronic course of their disease [4].

Cutaneous involvement in diabetes mellitus [DM] has been linked to a variety of pathomechanisms, which include disrupted carbohydrate metabolism, impaired host immune system, microangiopathy, atherosclerosis and neuro-degeneration [5]. Several common and rare cutaneous disorders associated with diabetes mellitus in the form of diabetic necrobiosis lipoidica, dermopathy, diabetic bullae, acanthosis nigricans, diabetic thick skin, yellow skin, eruptive xanthomas, scleroderma, yellow nails, skin tags, disseminated granuloma annulare, vitiligo and lichen planus [6]. Common cutaneous manifestations of type I diabetes that begin in the early stages of diabetes, such as acquired ichthyosis and keratosis pilaris [3].

Acanthosis nigricans is likely to be the most recognized cutaneous disorder of diabetes. It was present in up to 74% of adult obese diabetic patients [7, 8].

A Swedish study showed that, diabetic dermopathy presented in 33% of type-1 diabetes and 2% of the control group [9]. Folliculitis, furunculosis, carbuncle, ecthyma, erysipelas, and cellulitis are common cutaneous bacterial infections associated with diabetes. Pityriasis versicolor, dermatophytosis, and vulvovaginal candidiasis are the most common cutaneous fungal infections [10,11]. The commonest seen viral infections in diabetes are herpes zoster and viral warts [12].

THE AIM OF THE WORK

The current work aimed to estimate prevalence of cutaneous disorders in diabetic patients and to determine the associations between cutaneous disorders and the

patient's risk factors in the Damietta governorate

PATIENTS AND METHODS

This cross-sectional study was carried out among 947 patients with diabetes during the period from March 2020 to August 2021 the study participants were selected randomly from diabetic patients attending internal medicine out-patient clinics and chronic diseases out-patient clinics of the family health centers in different health care facilities from randomly selected three cities in Damietta governorate.

Patients of both sexes with diabetes mellitus, type I or type II, were included. But, patients with gestational diabetes were excluded.

Study Sample: The target population is diabetic patients in the Damietta governorate. By assuming that, the percentage of diabetic dermatoses among patients with diabetes is [35%] [13] at a confidence interval of 95%, with a study power was 90% by using EPI INFO the sample size will be [947] patients with diabetes.

All patients completed a questionnaire for socio-demographic characteristics of all patients including gender, age, residence, occupations, and level of education. A history taking was completed with stress on the duration of diabetes, mode of treatment for diabetes [diet only, oral hypoglycemic, insulin therapy, or combination therapy], and comorbidities. Then physical examination was performed and divided into general and dermatological examination. General examination included the measurement of weight and height and body mass index [BMI] was calculated. Then, patients were categorized into normal [18.5- 24.9 kg/m²], underweight [<18.5 kg/m²], overweight [25- 29.9 kg/m²], and obesity [\geq 30 kg/m²].

Dermatological disorders were searched for and a provisional clinical diagnosis was made. Some patients were diagnosed before and three of them did histopathology for confirmation of the diagnosis and they were on treatment. Dermoscopy and Woods lamp examination was used when required to confirm the diagnosis. Other cases needed a consultation for confirmation of diagnosis.

Investigation included the assessment of glycemic control [HbA1c] of the patients from their medical sheets. HbA1c less than 7% defined as a good control, and values greater than 7% indicates poor glycemic control.

Ethical consideration: Participation was voluntary and informed consent was taken prior to data collection. Ethical considerations and confidentiality were respected.

The research protocol was approved by the Damietta Faculty of Medicine, Al-Azhar University Institutional Review Board.

Statistical analysis: Data entry and statistical analysis was performed using SPSS [The Statistical Package for Social Sciences, version 21.0]. Descriptive analysis, frequency, and percentage for categorical data and mean \pm SD for continuous variables. Chi-square test was performed to test the association and/or difference between categorical variables. Fischer's exact test was applied instead of the chi-square test if the frequency in at least one cell is less than five. Student's t-test for comparing two means. Multiple regression analysis for detecting the predictors of diabetes disorders variables. P-value less than [0.05] was considered statistically significant.

RESULTS

Table [I] showed the demographic characteristics of the patients under the study. The total number was 947 patients and the mean \pm SD of the age was 51.05 \pm 7.08 years and the majority of them [85.9%] are between 40-60 years. Males account for about 42.0%. Females have a higher BMI than males with a statistically significant difference. Furthermore, 22.0% of studied patients had comorbidities.

Diabetes accounts for 98.2% of the studied patients. Only 7.6% [4.8% of males and 9.7 % of females] had a diabetes duration of less than five years while 47.9% [46.5 males and 49% of females] had diabetes duration between five to ten years and 44.5% [48.7% of males and 41.3% of females] had diabetes duration more than ten years. Hemoglobin A1C was uncontrolled in 79.6% of males and 71.9% of females with a significant difference. The studied patients had skin manifestations strongly associated with diabetes in the form of acanthosis nigricans [16.2], diabetic dermopathy [7.7], scleroderma-like skin changes [8.2%], scleredema

diabetocorum [0.4%], necrobiosis lipidica [0.2%] and diabetic foot ulcers [3%]. Acrochordons were the most prevalent nonspecific dermatological signs and symptoms associated with diabetes [19.2%] followed by pruritus [18.2%] and xerosis [16.6%]. While keratosis pilaris [6.1%], pigmented purpuric dermatoses [2.7%], eruptive xanthomas [1.9%], xanthelasma [1.4%], rubeosis faciei [1.2%], palmar erythema [1%] and yellow skin & nails [0.8%] were less prevalent. The prevalence of dermatologic diseases associated with diabetes was low in the form of psoriasis [0.95%], vitiligo [0.53%], and lichen planus [0.32%]. Fungal infections were prevalent among diabetics [21.3%] than bacterial infections [7.7%] and viral infections were present in 4.96% [Table II].

Uncontrolled diabetic patients are more prone to develop diabetic-associated dermatological disorders than controlled. Acanthosis nigricans, diabetic dermopathy, scleroderma-like skin changes, and pigmented purpuric dermatoses were strongly associated with uncontrolled diabetic patients with significant difference. Diabetic foot ulcers and xerosis were also associated with uncontrolled patients [Table III]. The longer the duration of diabetes mellitus, the higher the prevalence of acanthosis nigricans, diabetic dermopathy, scleroderma-like skin changes, xerosis, and pigmented purpuric dermatoses with highly statistically significant difference. Diabetic foot ulcers are also associated with a longer duration of DM [Table IV].

Multivariate logistic regression analysis showed that the independent risk factors of Skin manifestations strongly associated with study diabetic patients were obesity, type II diabetes, longer duration, and uncontrolled hemoglobin A1C [Table V].

Table [I]: the demographic and disease characteristics of the study participants.

	Male [398]	Female [549]	Total [947]	Test	P value
Age [years]	51.06 \pm 7.04	51.05 \pm 7.12	51.05 \pm 7.08	0.012	0.99
- 20-40	12 [3]	27 [4.9]	39 [4.1]	2.2	0.33
- 41-60	347 [87.2]	466 [84.9]	813 [85.9]		
- >60	39 [9.8]	56 [10.2]	95 [10.0]		
BMI	28.09 \pm 3.56	31.22 \pm 2.83	29.90 \pm 3.51	15.01	<0.001**
- Normal	85 [21.4]	13 [2.4]	98 [10.3]	157	<0.001**
- Overweight	192 [48.2]	170 [31]	362 [38.2]		
- Obese	121 [30.4]	366 [66.6]	487 [51.4]		
Type of diabetes					
- Type I	11 [2.8%]	6 [1.1%]	17 [1.8]	3.65	0.056
- Type II	387 [97.2%]	543 [98.9%]	930 [98.2]		
Duration of DM [year]	9.44 \pm 4.54	9.05 \pm 4.66	9.21 \pm 4.61	t= 1.28	0.198
- <5	19 [4.8]	53 [9.7]	72 [7.6]	10.37	<0.001**
- 5-10	185 [46.5]	269 [49]	454 [47.9]		
- >10	194 [48.7]	227 [41.3]	421 [44.5]		
Hemoglobin A1C	8.71 \pm 1.17	8.58 \pm 1.33	8.63 \pm 1.26	t= 1.51	0.13
- Controlled	81 [20.4]	154 [28.1]	235 [24.8]	7.33	<0.001**
- Uncontrolled	317 [79.6]	395 [71.9]	712 [75.2]		
Comorbidities	90 [22.6]	118 [21.5]	208 [22.0]	0.16	0.68

Table [II]: Prevalence of Skin manifestations associated with diabetes.

Disease	n. (947)	%
Infections	256	27.03
Fungal infection	202	21.3
Acrochordons	182	19.2
Pruritus	172	18.2
Xerosis	157	16.6
Acanthosis Nigricans	153	16.2
Scleroderma-Like Skin Changes [Thick Skin]	78	8.2
Bacterial infection	73	7.7
Diabetic Dermopathy	73	7.7
Keratosis Pilaris	58	6.1
Viral infections	47	4.96
Diabetic Foot ulcers	28	3.0
Pigmented Purpuric Dermatoses	26	2.7
Eruptive Xanthomas	18	1.9
Xanthelasma	13	1.4
Rubeosis Faciei	11	1.2
Ichthyosiform Changes of the Shins	10	1.1
Palmar Erythema	9	1
Psoriasis	9	0.95
Yellow Skin and Nails	8	0.8
Vitiligo	5	0.53
Scleredema Diabetocorum	4	0.4
Lichen Planus	3	0.32
Necrobiosis Lipoidica	2	0.2

Table [III]: Skin disorders in diabetic patients and their relationship with diabetes control

	Uncontrolled [712]	Controlled [235]	X ²	OR [95% CI]	P
Acanthosis Nigricans	134 [18.8]	19 [8.1]	15.03	2.19 [1.4-3.38]	<0.001**
Diabetic Dermopathy	72 [10.1]	1 [0.4]	15.85	4.82 [1.84-12.58]	<0.001**
Scleroderma-Like Skin Changes [Thick Skin]	76 [10.7]	2 [0.9]	22.55	10.45 [2.6-41.25]	<0.001**
Scleredema Diabetocorum	4 [0.6]	0	1.32	2.9 [0.16-55.7]	0.57
Necrobiosis Lipoidica	2 [0.3]	0	0.66	1.65 [0.07-34.64]	0.41
Diabetic Foot ulcers	26 [3.7]	2 [0.9]	4.82	3.55 [1.4-13.5]	0.028*
Ichthyosiform Changes of the Shins	8 [1.1]	2 [0.9]	0.12	1.24 [0.25-4.31]	0.72
Xerosis	129 [18.1]	28 [11.9]	4.91	1.46 [1.03-2.09]	0.027*
Eruptive Xanthomas	11 [1.5]	7 [3]	1.94	0.63 [0.35-1.13]	0.16
Xanthelasma	12	1	2.07	3.25 [0.49-21.4]	0.15
Acrochordons	129 [18.1]	53 [22.6]	2.23	0.81 [0.63-1.05]	0.13
Pruritus	124 [17.4]	48 [20.4]	1.07	0.86 [0.66-1.13]	0.29
Keratosis Pilaris	43 [6]	15 [6.4]	0.036	0.95 [0.61-1.50]	0.84
Pigmented Purpuric Dermatoses	26 [3.7]	0 [0.0]	8.82	18.18 [1.103-29.5]	<0.001**
Palmar Erythema	8 [1.1]	1 [0.4]	0.91	2.25 [0.35-14.29]	0.33
Rubeosis Faciei	7 [1]	4 [1.7]	0.79	0.67 [0.3-1.49]	0.37
Yellow Skin and Nails	6 [0.8]	2 [0.9]	0.01	0.99 [0.29-3.3]	0.9
Infections	236 [33.1]	20 [8.5]	54.36	3.98 [2.57-6.15]	<0.001**

*Significant [P<0.05], **highly significant [P<0.01]

Table [IV]: Dermatological disorders among studied diabetic patients and their association with disease duration.

	<5	5-10	>10	X ²	p
Acanthosis Nigricans	5 [6.9]	64 [14.1]	84 [20]	10.41	0.005**
Diabetic Dermopathy	0	4 [0.9]	69 [16.4]	80.35	<0.001**
Scleroderma-Like Skin Changes [Diabetic Thick Skin]	0	19 [4.2]	59 [14]	34.91	<0.001**
Scleredema Diabetocorum	0	0	4	5.01	0.81
Necrobiosis Lipoidica	0	0	2 [0.5]	2.5	0.28
Diabetic Foot ulcers	0	8 [1.8]	20 [4.8]	9.17	0.01*
Ichthyosiform Changes of the Shins	0 [0]	7 [1.5]	3 [0.7]	2.29	0.32
Xerosis	9 [12.5]	50 [11]	98 [23.3]	24.69	<0.001**
Eruptive Xanthomas	0	9 [2]	9 [2.1]	1.53	0.46
Xanthelasma	0	4 [0.5]	9 [2.1]	3.63	0.16
Acrochordons	19 [26.4]	86 [18.9]	77 [18.3]	2.64	0.26
Pruritus	17 [23.6]	76 [16.7]	79 [18.8]	2.15	0.3
Keratosis Pilaris	5 [6.9]	25 [5.5]	28 [6.7]	0.58	0.74
Pigmented Purpuric Dermatoses	0	2 [0.4]	24 [5.7]	24.83	<0.001**
Palmar Erythema	0	4 [0.9]	5 [1.2]	0.96	0.61
Rubeosis Faciei	0	8 [1.8]	3 [0.7]	3.01	0.22
Yellow Skin and Nails	1 [1.4]	3 [0.7]	4 [1]	0.49	0.78
Infections	0	73 [16.1]	183 [43.5]	111.94	<0.001**

*Significant [P<0.05], **highly significant [P<0.01]

Table [V]: Multivariate logistic regression analysis of risk factors associated with Skin manifestations strongly associated with diabetes.

	B	S.E.	Wald	Sig.	OR	95% C.I. for OR	
						Lower	Upper
BMI	0.146	.027	28.725	0.001**	1.157	1.097	1.220
Type II diabetes	2.770	1.115	6.173	0.013*	15.961	1.795	141.939
Sex [Female]	-.271-	0.181	2.246	0.134	0.763	0.535	1.087
Duration	0.105	0.020	26.173	0.001**	1.111	1.067	1.156
Hemoglobin A1C [Uncontrolled]	0.513	0.266	3.733	0.048*	1.671	1.13	2.811
Comorbidities	0.195	0.188	1.076	0.300	1.216	0.841	1.759

*Significant [P<0.05], **highly significant [P<0.01]

DISCUSSION

The skin provides a window into what is happening inside the body so cutaneous manifestations could be a reflection of a serious health problem and a marker of internal diseases [14]. DM is a chronic syndrome manifested by hyperglycemia due to relative or absolute insulin deficiency. Cutaneous disorders of DM usually appear following the onset of the disease; however, it may be the first presenting sign and, in some cases, may occur many years before the primary disease manifestation [15].

In this study, the most prevalent cutaneous disorder among the studied diabetic patients was cutaneous infections [27%], the prevalence of fungal infections was 21.3%, bacterial infections were 7.7%, and viral infections presented in 4.96%. This result was in accordance with that of Girisha and Viswanathan [16] where fungal infection was presented in 106 [26.5%] patients and bacterial infections were presented in 27[6.75%] patients. A higher prevalence of cutaneous infections was found in an observational study from a tertiary care hospital by Baidya *et al.* [17] that was in 50% of cases.

Our study revealed a strong association between cutaneous infection and poorly controlled diabetes and a longer duration of diabetes. Hyperglycemia impairs host defenses by causing functional abnormalities in leucocytes, resulting in decreased leukocyte response and impaired phagocytosis. Chemotaxis is reduced by hyperosmolar serum, and insulin deficiency impairs cytokine release [18].

Acrochordons are asymptomatic, pedunculated, polypoid structures found mainly in the intertriginous areas that are strongly linked to diabetes and insulin resistance [19]. The current study revealed that the second most common dermatoses among patients with diabetes was acrochordons which presented in 182 [19.2%]. A lower prevalence was reported by Vathsala *et al.* [20] who examined 500 patients in a tertiary care, it was in 14.4%. A higher prevalence was recorded by Mahajan *et al.* [21] acrochordons were manifested in 32% of patients.

In our study, pruritus was the third common manifestation presented in [18.2%] of the study participants. In a study by Niaz *et al.* [6] pruritus was presented in 8% of examined diabetes patients. According to a study in Kuwait on 106 diabetic patients, pruritus presented in 47% of them [22].

Chatterjee *et al.* [23] in their study revealed that pruritus was the most common presenting symptom and seen in 60.23% of patients.

We found that pruritus did not correlate with glycemic control, the duration of diabetes, and gender. In diabetes, pruritus is due to xerosis, diabetic nephropathy, neuropathy, and use of the antidiabetic drugs [24]. Diabetic polyneuropathy with correlated sweating dysfunction may play a role in the pathogenesis of diabetic pruritus [25].

In our study, xerosis was presented in 16.6% of the group being studied. The pathogenesis of ichthyosis, xerosis, and pruritus has been linked to a decreased hydration state of the stratum corneum, decreased sebaceous gland activity in diabetic patients, and autonomic neuropathy. [26].

Acanthosis nigricans manifested in 16.2% of our diabetic patients. This associated dermatological feature was less common than infection and this is due to insulin resistance. keratinocytes and fibroblasts express [IGF] receptors that bind insulin and have growth-promoting effects. Decreased numbers of functional insulin receptors cause a shift to increased binding to IGF receptors, which contributes to the development of acanthosis nigricans [27]. Scleroderma-like skin changes was presented in 8.2% of our participants with diabetes and it was strongly associated with uncontrolled diabetic patients with highly significant difference [p<0.001]. In our study, diabetic dermopathy was diagnosed in 7.7% of diabetic patients. A similar finding was reported in a recent study on 100 diabetic patients that present in 7% [28], while a higher prevalence was reported in many studies ranging from 15% to 40% [29-31].

The diabetic foot syndrome is an important cutaneous manifestation seen in 15–25% of diabetic patients [32], which was more than our study [3%]; it may due to the lower mean duration of diabetes in our study. In the development of diabetic foot syndrome, a combination of disturbed sensation and vasculopathy play crucial roles [24]. The longer duration of diabetes, poor controlled hemoglobin A1C and obesity were independent risk factors of skin manifestations strongly associated with diabetes.

Conclusion: Cutaneous disorders among diabetic patients are prevalent. The most common disorders are cutaneous infections, acrochordons, pruritus, xerosis, acanthosis nigricans, scleroderma-like skin changes, and diabetic dermopathy. Cutaneous manifestations of

diabetes can emerge prior to the diagnosis of diabetes and may reflect glycemic control and other neuro-vascular complications; increasing the awareness of the clinicians about this problem will help in the more comprehensive management of diabetes and dermatoses, as well as early diagnosis and prevention of diabetes complications.

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None

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