Short Communication

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Frequency of Cutaneous Manifestations in Diabetic Patients in Endocrinology Clinic of Babol University of Medical Sciences

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ABSTRACT

BACKGROUND AND OBJECTIVE: Diabetes is the most common endocrine disorder in the world. Understanding the cutaneous manifestations associated with diabetes can help in choosing the appropriate treatment approach in these patients. The aim of this study was to evaluate the frequency of cutaneous manifestations in diabetic patients referred to the endocrinology clinic of Babol University of Medical Sciences.

METHODS: The present cross-sectional study was performed on 300 patients with diabetes referred to Rouhani Hospital in Babol in 2019. Age, gender, BMI, type and duration of diabetes, and patients' diabetes control status (HbA1C) were recorded and patients were thoroughly examined by a dermatologist and divided into two groups of below and above 50 years. In terms of cutaneous manifestations, they were divided into two groups; with cutaneous manifestations and without cutaneous manifestations.

FINDINGS: 293 patients (97.76%) had type 2 diabetes. The mean age of patients was 55±12 years and the mean duration of diabetes was 9.73±1.20 years. In this study, 130 patients (43%) had cutaneous lesions, of which 76 patients (58.5%) were female. Pruritus, acrochordon, cherry angioma, diabetic dermatopathy, fungal skin infections with frequencies of 25.7%, 21%, 14.3%, 6% and 5.7% were the most common skin disorders, respectively. 68 patients (69.4%) had skin manifestations and had diabetes for more than 10 years. There was a significant difference between the two groups of with and without cutaneous manifestations, gender and duration of diabetes ($p<0.001$). There was no significant difference between the mean age, BMI and HbA1C in the two groups ($p=0.07$, $p=0.09$ and $p=0.11$, respectively).

CONCLUSION: The results of the study showed that pruritus and acrochordon are the most common cutaneous manifestations and long-term diabetes and female gender are the most important risk factors for cutaneous manifestations.

KEY WORDS: *Diabetes Mellitus, Glandular Disease, Cutaneous Manifestations.*

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Introduction

Diabetes is the most common glandular disease in the world and is responsible for about 4 million deaths per year (1). Diabetes is a growing public health concern. Most of the importance of diabetes is due to its high prevalence and the numerous complications that follow (2, 3). Given the growing statistics and trends of diabetes in the world, it can be declared a latent epidemic. The global prevalence of diabetes is estimated to reach 552 million by 2030 (3, 4).

This disease can affect all systems of the body, including the skin. Cutaneous manifestations of diabetes can be divided into three categories: diabetes-related skin diseases (necrobiosis lipoidica, diabetic dermatopathy, acrochordon or skin tag, diabetic scleroderma, eruptive xanthomas, perforating dermatoses, acanthosis nigricans, dry skin, diabetic blisters, granuloma annulare, skin infections [bacterial or fungal]), skin manifestations due to complications of diabetes (microangiopathy, macroangiopathy and neuropathy) and skin complications due to diabetes treatment (sulfonylureas and insulin) (5-7).

According to various studies, 30-82% of patients with diabetes mellitus have cutaneous manifestations during the course of the disease (8). Hyperglycemia leads to non-enzymatic glycosylation of various structural and regulatory proteins, including collagen. This non-enzymatic glycosylation leads to the production of advanced glycation end products (AGEs), which causes various cutaneous disorders such as ichthyosis vulgaris and limited joint mobility (diabetic cheiroarthropathy) in diabetic patients (9, 10). Pathological blood sugar levels severely affect skin homeostasis. The consequences of this change in skin homeostasis include inhibition of keratinocyte proliferation and migration, impaired protein biosynthesis and issues such as epithelial cell apoptosis, etc. (9, 11, 12).

The etiopathology of skin and systemic infections in diabetic patients is related to changes in the immune regulatory system such as disorders of chemotaxis and phagocytosis and decreased cellular immunity. Metabolic disorders such as hyperinsulinemia are seen in the early stages of type 2 diabetes, with an effect on the receptor for insulin-like growth factor 1 (IGF-1) that leads to abnormal proliferation of epidermal cells and the formation of the acanthosis nigricans phenotype (10, 13-15). In diabetic patients with insulin deficiency, the abnormal activity of lipoprotein lipase is caused by a defect in lipid processing and can lead to severe hypertriglyceridemia, which manifests itself in the skin as eruptive xanthomas. Macro- and micro-angiopathy are significantly associated with the skin complications of diabetes (2, 10, 16, 17). In addition, loss of skin nerve can occur in diabetes. Peripheral neuropathy in diabetes, along with other complications such as angiopathy and infection, leads to diabetic foot ulcers (7). Drug response in diabetic patients is in the form of local reactions to insulin, which are in three types of immediate local reaction, immediate generalized reaction, and delayed reaction, which is more common than the previous two forms and two weeks after insulin treatment, it appears as an itchy nodule at the injection site and heals within a few days while leaving a scar (16-18).

Recognizing cutaneous lesions not only helps to diagnose diabetes in some cases, but in some cases raises the possibility of complications in other important organs. On the other hand, prevention and treatment of many cutaneous lesions prevent their progression and are effective in reducing the patient's disability and socioeconomic injuries (19-22). The aim of this study was to evaluate the cutaneous manifestations in diabetic patients.

Methods

This cross-sectional study was performed on patients with diabetes after approval by the ethics committee of Babol University of Medical Sciences with the code IR.MUBABOL.HRI.REC.1398.312. In this study, 300 patients with diabetes who referred to the endocrinology clinic of Rouhani Hospital in 2019 after endocrinologist visit and after expressing consent were included in the study. Demographic information of patients such as age, gender, BMI, type and duration of diabetes, and patients' diabetes control status (HbA1C) were recorded and then patients underwent full skin examination by a dermatologist.

Diagnosis of cutaneous lesions was based on clinical examination and in suspected cases, paraclinical tests and biopsy were used. All cutaneous manifestations, including diabetes-related cutaneous diseases, cutaneous infections, cutaneous complications due to diabetes, and reactions of skin to diabetes treatment were examined and recorded. Skin burn lesions were excluded from the study. In terms of cutaneous manifestations, patients were divided into two groups with and without manifestations. After coding, the collected data were analyzed in SPSS V. 24 statistical

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software using Fisher's exact tests, Pearson correlation coefficient and $p<0.05$ was considered significant.

Results

In this study, out of 300 diabetic patients, 130 patients had cutaneous manifestations. Pruritus was the most common cutaneous manifestation with a frequency of 25.7% (Table 1).

Table 1. Frequency distribution of skin disorders in diabetic patients referred to endocrinology clinics of Babol University of Medical Sciences

Type of cutaneous manifestation	Number(%)
Pruritus	77(25.7)
Acrochordon	63(21)
Cherry angioma	43(14.3)
Diabetic dermopathy	18(6)
Fungal diseases	17(5.66)
Xerosis	14(4.66)
Seborrheic keratosis	12(4)
Eczema	3(1)
Acanthosis nigricans	3(1)
Diabetic foot	3(1)
Alopecia areata	2(0.7)
Bullous diabeticorum	2(0.7)
Pityriasis versicolor	2(0.7)
Pigmented purpuric dermatosis	2(0.6)
Psoriasis	1(0.3)
Urticaria	1(0.3)
Diabetic scleroderma	1(0.3)
Cystic acne	1(0.3)
Lichen Planus	1(0.3)
Vitiligo	1(0.3)
Herpes zoster	1(0.3)
Granuloma annulare	1(0.3)

Of these 130 patients, 54 (41.5%) were male and 76 (58.5%) were female. A statistically significant relationship was found between gender and the incidence of cutaneous manifestations in diabetic patients ($p<0.001$). The mean age of patients was 55.01±12.06 years. Patients were divided into two groups of below and above 50 years. Except for alopecia areata, in which both patients were under 50 years of age, in other cases there was no significant difference between below and above 50 years ($p=0.07$).

293 patients (97.76%) had type 2 diabetes and 7 patients (2.24%) had type 1 diabetes. The mean duration of diabetes was 9.73±8.20 years. 68 patients (69.4%) with diabetes who had been diagnosed for more than 10 years had cutaneous lesions. 140 patients (69.3%) had no cutaneous lesions, which was statistically significant ($p=0.001$). The mean hemoglobin A_1C in all patients in this study was 8±1.7. Mean HbA_1C was not significantly different between the two groups of with and without cutaneous manifestations ($p=0.11$). The mean BMI of patients in this study was 27.5±4.8 kg/m2 and 72.7% of patients had a BMI above 25. There was no significant difference between BMI and the type of cutaneous disorder ($p=0.09$). No cutaneous manifestations related to subcutaneous insulin injection were observed among patients.

Discussion

In this study, 130 patients (43%) had cutaneous lesions, of which 76 patients (58.5%) were females and pruritus and acrochordon with frequencies of 25.7% and 21% were the most common cutaneous disorders. In this study, cutaneous manifestations were seen in 43% of patients. In the studies of Bhardwaj et al., Demirseren et al., Fatima et al. and Golfooroshan et al., the frequency of cutaneous manifestations in diabetic patients was 73%, 64%, 79.2% and 16%, respectively (17, 18, 22, 23).

Inconsistency in the results may be due to differences in the study population and the fact that the present study is a cross-sectional one. In the present study, most patients with cutaneous lesions were women (58.5% vs. 41.5%). In many studies, the majority of patients were women, which is in line with the results of our study (17, 24, 25). However, in some studies such as Golforoushan et al., the frequency of men was higher than women (57.5%) (23). This difference may be due to differences in the population studied. In the present study, most patients (97.76%) had type 2 diabetes, which is in line with previous research (1).

In our study, 72.7% of patients had a BMI above 25. One of the risk factors for diabetes is obesity, which is based on the increase in BMI. In various studies, a BMI above 30 is considered obesity. In a study conducted in 2019 by Basterra-Gortari et al., the prevalence of obesity in diabetic patients at different ages ranged from 18.2 to 42% (26). In the study of Zhou et al., the prevalence of obesity in diabetic patients was 16% (27). In the present study, the prevalence of obesity in diabetic patients was 26%, which was higher than the study by Zhou et al. and close to the range reported by Basterra-Gortari et al. In the present study, pruritus, acrochordon, cherry angioma, diabetic dermatopathy, fungal skin infections with frequencies of 25.7%, 21%, 14.3%, 6% and 5.7% were the most common skin disorders, respectively. In a study on 200 diabetic

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patients in 2002, dermatophytes and candida fungal infections were the most common cutaneous manifestations in 23 patients (11.5%) and 22 patients (11%), respectively. Diffuse itch (10.5%) and acanthosis nigricans (10%) were also common skin cases (28). In a study on 377 diabetic patients, common skin manifestations included fungal and bacterial infections, itch, xerosis, diabetic dermatopathy, and less common manifestations included necrobiosis lipoidica, alopecia areata, diabetic scleroderma, and granuloma annulare.

In the study of Niaz et al., the most common disorder was bacterial cutaneous infection (26%), followed by fungal infections and acanthosis nigricans and diabetic foot with a prevalence of 22%, 20% and 16%, respectively (24). In the study of Farshchian et al., after cutaneous infections (37.9%), diffuse or localized itch (28.1%) and acrochordon (19.1%) were the most common cutaneous manifestations in diabetic patients (25). The most common causes of cutaneous infections in diabetic patients are impaired release of cytokines due to lack of insulin, phagocytic disorders, increased mast cells in the upper dermis and increased glucose levels (9, 26, 29).

Considering the fact that in our study, unlike previous studies, cutaneous infections were not the most common finding, we can point out the difference in the type of studies; the present research is a cross-sectional study, while studies with longer follow-up are likely to have higher rates of cutaneous infections than other complaints, and that our patients were outpatients, while many of these studies included hospitalized patients and outpatients. In the present study, pruritus was reported as the most common cutaneous symptom. The prevalence of pruritus in the study of Farshchian et al. was 28.1%, and in the study of Derakhshan et al. was 23.8%, which is similar to the present study (25, 30). In the study of Bhardwaj, the prevalence of pruritus was 12.5% and in the study of Raghuet al. was 14% (17, 31). The reason for differences in different reports, in addition to differences in the studied samples (associated underlying diseases, duration of diabetes, level of diabetes control, etc.), can be due to differences in scientific definitions of pruritus, types of pruritus and its association and lack of association with other cutaneous disorders.

In the present study, more cutaneous manifestations were seen in patients with diabetes over 10 years (69.4%), and the relationship between the duration of diabetes for more than 10 years and the frequency of cutaneous manifestations was statistically significant ($p<0.001$), which was similar to studies conducted by Shemer et al. as well as Diris et al. (32, 33). However, no significant relationship was found between cutaneous manifestations and age, HbA1C and BMI. Nevertheless, in the study of Shemer et al., there was a significant relationship between cutaneous manifestations and HbA1C, which could be due to the high mean HbA1C in our study population.

The results of the study showed that pruritus and acrochordon are the most common cutaneous manifestations and long-term diabetes and female gender are the most important risk factors for cutaneous manifestations.

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References

1.Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. Nat Rev Endocrinol. 2018;14(2):88-98.

2.Chawla A, Chawla R, Jaggi S. Microvasular and macrovascular complications in diabetes mellitus: distinct or continuum?. Indian J Endocrinol Metab. 2016;20(4):546-51.

3.Glovaci D, Fan W, Wong ND. Epidemiology of diabetes mellitus and cardiovascular disease. Curr Cardiol Rep. 2019;21(4):21.

4.Petersmann A, Nauck M, Müller-Wieland D, Kerner W, Müller UA, Landgraf R, et al. Definition, classification and diagnosis of diabetes mellitus. Exp Clin Endocrinol Diabetes. 2018;126(7):406-410.

5.Mauri-Obradors E, Estrugo-Devesa A, Jané-Salas E, Viñas M, López-López J. Oral manifestations of Diabetes Mellitus. A systematic review. Med Oral Patol Oral Cir Bucal. 2017;22(5):e586-e94.

6.Ferringer T, Miller OF. Cutaneous manifestatuions of diabetes melitus. Dermatol Clin. 2002;20(3):483-92.

7.Asadi M, KHorasani G-A. Diabetic Foot. J Clin Exc. 2013;1(2):17-34. [In Persian]

8.Freinkel RK. Cutaneous mainfestations of endocrine diseaes. In: Fitzpatrick TB, Eisen AZ, Wollt K, Freedberg IM, Austen KF, editors. Dermatology in General Medicine, 4th ed. New York, USA: McGraw-Hill; 1993.p. 2123-31.

9.Jobbour SA, Miller JL. Endocrinopathies and the skin. Int J Dermatol. 2000;39(2):88-99.

10.Jetinek JE. Cutaneas manifestations of diabetes mellitus. Int J Dermatol. 1994;33(9):605-17.

11.de Macedo GM, Nunes S, Barreto T. Skin disorders in diabetes mellitus: an epidemiology and physiopathology review. Diabetol Metab Syndr. 2016;8(1):63.

12.Sanches MM, Roda Â, Pimenta R, Filipe PL, Freitas JP. Cutaneous Manifestations of Diabetes Mellitus and Prediabetes. Acta Med Port. 2019;32(6):459-65.

13.Mistry BD, Alavi A, Ali S, Mistry N. A systematic review of the relationship between glycemic control and necrobiosis lipoidica diabeticorum in patients with diabetes mellitus. Int J Dermatol. 2017;56(12):1319-27.

14.Mahmood T, ul Bari A, Agha H. Cutaneous manifestations of diabetes mellitus. J Pakistan Associate Dermatol. 2005;15(3):227-32.

15.Makrantonaki E, Jiang D, Hossini AM, Nikolakis G, Wlaschek M, Scharffetter-Kochanek K, Zouboulis CC. Diabetes mellitus and the skin. Rev Endocr Metab Disord. 2016;17(3):269-82.

16.González-Saldivar G, Rodríguez-Gutiérrez R, Ocampo-Candiani J, González-González JG, Gómez-Flores M. Skin manifestations of insulin resistance: from a biochemical stance to a clinical diagnosis and management. Dermatol Ther (Heidelb). 2017;7(1):37-51.

17.Bhardwaj N, Roy S, Jindal R, Ahmad S. Cutaneous manifestations of diabetes mellitus: a clinical study. Int J Res Dermatol. 2018;4(3):352-6.

18.Demirseren DD, Emre S, Akoglu G, Arpacı D, Arman A, Metin A, et al. Relationship between skin diseases and extracutaneous complications of diabetes mellitus: clinical analysis of 750 patients. Am J Clin Dermatol. 2014;15(1):65-70.

19.Alwaash SS, Al-Shibly K. Dermatological Manifestations of Diabetes Mellitus in Hilla City. Med J Babylon. 2017;14(3):495-500.

20.Horton WB, Boler PL, Subauste AR. Diabetes Mellitus and the Skin: Recognition and Management of Cutaneous Manifestations. South Med J. 2016;109(10):636-46.

21.Tolliver S, Graham J, Kaffenberger BH. A review of cutaneous manifestations within glucagonoma syndrome: necrolytic migratory erythema. Int J Dermatol. 2018;57(6):642-5.

22.Fatima K, Naheed A, Amir Khan S. Skin Manifestations of Diabetes Mellitus. J Rawalpindi Med Coll. 2018;22(3): 252-255.

23.Golfooroshan F, Khodaeiani E, Babaei Nejad S, Laghosi D. Skin Lesions in Diabetic Patients Refering to Dermatology and Diabetes Clinic of Sina Hospital, Tabriz. J Ardabil Univ Med Sci. 2006;6(2):170-5. [In Persian]

24.Niaz F, Bashir F, Shams N, Shaikh Z, Ahmed I. Cutaneous manifestations of diabetes mellitus type 2: prevalence and association with glycemic control. J Pakistan Associate Dermatol. 2016;26(1):4-11.

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[DOI: 10.22088/jbums.23.1.380]

25.Farshchian M, Farshchian M, Fereydoonnejad M, Yazdanfar A, Kimyai-Asadi A. Cutaneous manifestations of diabetes mellitus: a case series. Cutis. 2010;86(1):31-5.
26.Basterra-Gortari FJ, Bes-Rastrollo M, Ruiz-Canela M, Gea A, Sayón-Orea C, Martínez-González MÁ. Trends of obesity prevalence among Spanish adults with diabetes, 1987-2012. Med Clin (Barc). 2019;152(5):181-4.
27.Zhou X, Ji L, Ran X, Su B, Ji Q, Pan C, et al. Prevalence of obesity and its influence on achievement of cardiometabolic therapeutic goals in chinese type 2 diabetes patients: an analysis of the nationwide, cross-sectional 3B study. PLoS One. 2016;11(1):e0144179.
28.Yadav S, Goyal A, Verma P. Pattern of Cutaneous Manifestations of Diabetes Mellitus. Paripex-Indian J Res. 2020;9(1):4-6.
29.Mendes AL, Miot HA, Haddad Junior V. Diabetes mellitus and the skin. An Bras Dermatol. 2017;92(1):8-20.
30.Derakhshan R, Khoshnood A, Balaee P. Evaluation of Abdominal Obesity Prevalence in Diabetic Patients and Relation with Other Factors of Metabolic Syndrome. Iran J Endocrin Metab. 2010;12(3):208-12. [In Persian]
31.Raghu TY, Vinayak V, Kanthraj GR, Girisha BS. Study of cutaneous maintestations of diabetes mellitus. Indian J Dermatol. 2004;49(2):73-5. Available from: https://www.e-ijd.org/article.asp?issn=0019-5154;year=2004;volume=49;issue=2;spage=73;epage=75;aulast=Raghu;type=0
32.Shemer A, Bergman R, Linn S, Kantor Y, Friedman-Birnbaum R. Diabetic dermopathy and internal complications in diabetes mellitus. Int J Dermatol. 1998;37(2):113-5.
33.Diris N, Colomb M, Leymarie F, Durlach V, Caron J, Bernard P. [Non infectious skin conditions associated with diabetes mellitus: a prospective study of 308 cases] . Ann Dermatol Venereol. 2003;130(11):1009-14.

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