Common Skin Disorders Associated with Type 2 Diabetes Mellitusin in Thi-Qar Province, Iraq

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History:

- Received: March 19, 2020
- Accepted: June 25, 2020
- Published: Sept 1, 2020

DOI: https://doi.org/10.31838/ejmcm.07.02.04

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INTRODUCTION

Diabetes mellitus (DM) is a clinical syndrome characterized by hyperglycaemia due to absolute or relative insulin deficiency(Shaikh *et al.*, 2006).Diabetes Mellitus is categorized into two types, DM type 1 (insulin dependent diabetes-IDDM) and DM type 2 (non-insulin dependent diabetes NIDDM) (Ahmed *et al.*, 2009).

Diabetes can have clinical manifestations in every organ system in the body, including the skin (Murphy-Chutorian et al., 2013). Skin disorders are common in both type 1 and type 2 diabetes but are more commonly seen in type 2 (Chatterjee et al., 2014). The skin is influenced by the acute metabolic derangements and the chronic degenerative complications of diabetes. Although the mechanism for many diabetes-associated skin conditions remains unknown, the pathogenesis of others is linked to abnormal carbohydrate metabolism, other altered metabolic pathways, atherosclerosis, microangiopathy, neuron degeneration, and impaired host mechanisms (Bhatet al., 2006). 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 (Naheed et al., 2002). Recent studies on diabetic patients have observed an increased incidence (ranging 20-50%) of skin infections (Van Hattem et al., 2008). The cutaneous manifestations of Diabetes Mellitus can be classified in four categories: 1- Skin disease with strong to

ABSTRACT

The current study was designed to determine the prevalence of skin disorders associated with type 2 diabetes mellitus which conducted from beginning of February 2019 to the end of march 2020. This study was carried out on 122 type 2 diabetic patients who visited the outpatients clinics of dermatology and venerology in Al-Hussein Teaching hospital in AL-Nasiriyah city, Thi-Qar province, Iraq. From 122 diabetic patients, 60(49.18%) males and 62(50.81%) females. Mean age was 58.63±9.42. The duration of diabetes mellitus with mean 6.73±3.3. The mean levels of RBS was found (257.43±75.77) mg/dL, FBS (147.79±26.62) mg/dL, HbAlc (8.76±1.61%). The present study demonstrate that the most considerably skin disorders was, bacterial infection 34 (27.86%), fungal infection 20 (16.39%), acanthosis nigricans 11(9.1%) whereas other skin disorders was less frequently in this study such as granuloma annulare, rubeosis, vitiligo, xerosis and yellow skin. The bacterial infection in males was recorded 24(40%) higher percentage among skin disorders while fungal infection in females 13 (20.96%) was more than other skin disorders. A significant differences between males and females in some skin disorders were observed in this study (P≤0.05). A significant differences were observed between pattern of skin disorders and values of RBS, FBS and HbAlc in diabetic patients (P≤0.05). According to type of treatment, a significant differences were recorded between type of skin disorders and combination therapy and oral hypoglycemic in diabetic patients (P≤0.05) while did not show significant difference in insulin therapy.

Keywords: Skin disorders, type 2Diabetes mellitus, Thi-Qar province.

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) (Sasmaz *et al.*, 2005).

While all other complications of diabetes mellitus have been extensively studied, the aspect of cutaneous manifestations and complications is relatively unexplored. There is no study explained the data linked to skin disorders in diabetic patients in Thi-Qar province southern of Iraq. For that reason the present study was designed to determine the prevalence and pattern of skin disorders among diabetic patients as first report.

PATIENTS AND METHODS

Patients population

The current study was carried out on 122 patients were involved in this study who visit the outpatients of dermatology and venereology in Al-Hussein Teaching hospital in Thi-Qar province / Iraq. The period of study was continued from beginning of February 2019 to the end of march 2020. Patients previously diagnosed to be suffering from type 2 diabetes mellitus presenting with skin disorders were included in the study. A questionnaire for demographic and clinical data was designed to include the patients age, gender, duration of Diabetes mellitus (years), mode of Diabetes mellitus treatment (insulin therapy, oral hypoglycemic and combination therapy), diet control only, Random Blood Sugar (mg/dL), Fasting Blood Sugar (mg/dL), HbA1c,s.creatinine (mg/dL), blood urea (mg/dL).

Ethic Approval

Ethic statements for this study were accepted by the patients and ethical committee.

Statistical analysis

ANOVAs and Chi-square tests were used for analysis the data in this study in SPSS software. P-value (≤ 0.05) was considered significant.

RESULTS

The present study was carried out on 122 patients who is suffering from skin disorders associated with diabetes mellitus. From all patients, the percentage of infection in males was 60(49.18%) and females 62(50.81%). The age of diabetic patients ranged from 35 - 81 years with mean age 58.63 ± 9.42 . The duration of diabetes mellitus with mean 6.73 ± 3.3 . According to the mode of diabetes mellitus treatment, oral hypoglycemic was higher 57 (46.72%) in treatment of diabetic patients followed by 38 (31.14%) for insulin therapy and 26 (21.31%) for combination therapy while diet control only was less average 1 (0.81%).

The present results showed that the mean levels of RBS was found (257.43 ± 75.77) mg/dL (range from 145 – 512), FBS (147.79±26.62) mg/dL (range from 92 – 212), HbAlc (8.76±1.61%) (Range from 6.5 – 13.1%), s.creatinine (0.95±0.24) mg/dL (range from 0.7 – 2.2), blood urea (15.8±8.43) mg/dL (range from 7 – 67). Table (1).

Table 1: Participants" characteristics of this study

Parame	ter	Mean ± SD	
age (year	rs)	58.63±9.42	
gender			
male		60(49.18)	
female		62(50.81)	
duratior	n of DM (years)	6.73±3.3	
mode of	DM treatment		
insulin t	herapy	38(31.14%)	
oral hyp	oglycemics	57(46.72%)	
combina	ition therapy	26(21.31%)	
diet cont	trol only	1(0.81%)	
RBS (mg	J/dL)	257.43±75.77	
FBS (mg	/dL)	147.79±26.62	
HbA1c%	D	8.76±1.61	
s. creatir	nine (mg/dL)	0.95±0.24	
blood ur	rea (mg/dL)	15.8±8.43	

In the present study, bacterial infection was the most common skin disorder associated with diabetes mellitus 34(27.86%) followed by fungal infection 20(16.39%) and acanthosis nigricans 11(9.1%) while other skin disorders such as granuloma annulare, perforating disorder, Reobiosis, vitiligo, xerosis and yellow skin were noticed less prevalence when compared with other skin disorders in diabetic patients. Statistically, significant differences were observed among skin disorders related to diabetes mellitus. The

current results showed that the significant differences were observed between males and females in some of skin disorders in diabetic patients such as bacterial infection, granuloma annulare, perforating disorder, Reobiosis, vitiligo, xerosis and yellow skin while did not show significant differences in other skin disorders. The values of infection percentage for males and females with P. value explained in table (2).

	Table 2: Prevalence of skir	disorders in diabetic p	patients (both males and females).
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Presenting disease	N=122 (%)	Male n=60 (%)	Female n=62 (%)	Pvalue
bacterial infection	34(27.86)	24(40)	10(16.12)	0.016
viral infection	10(8.19)	4(6.66)	6(9.76)	0.527
fungal infection	20(16.39)	7(11.66)	13(20.96)	0.180
Acanthosis nigricans	11(9.1)	5(8.33)	6(9.76)	0.763
Acrochordon	9(7.37)	3(5)	6(9.76)	0.317

pruritus	7(5.73)	4(6.66)	3(4.83)	0.705
diabetic bullae	2(1.63)	1(1.66)	1(1.61)	1.00
diabetic dermopathy	4(3.27)	1(1.66)	3(4.83)	0.317
diabetic foot	5(4.09)	3(5)	2(3.22)	0.655
granuloma annulare	1(0.81)	1(1.66)	0.00	0.00
lichen planus	2(1.63)	1(1.66)	1(1.61)	1.00
macular amyloidosis	2(1.63)	0.00	2(3.22)	0.00
nail changes	6(4.91)	1(1.66)	5(8.06)	0.102
Necrobiosis lipoidica	4(3.27)	2(3.33)	2(3.22)	1.00
perforating disorder	1(0.81)	1(1.66)	0.00	0.00
Rubeosis	1(0.81)	0.00	1(1.61)	0.00
vitiligo	1(0.81)	1(1.66)	0.00	0.00
xerosis	1(0.81)	1(1.66)	0.00	0.00
yellow skin	1(0.81)	0.00	1(1.61)	0.00
Total	122(100)	60(49.18)	62(50.82)	0.856

(P≤0.05)



Pic 1: Necrobiosis lipoidica.

Pic 2: Lichen planus and Vitiligo.



Pic 3: Diabetic bullous.

Pic 4: Acanthosis nigricans.

The current study showed that the highest mean of disease duration was in the diabetic patients with nail change (8.33 ± 3.26) and the lowest mean was in the diabetics with diabetic foot (5.40 ± 2.60) with no significant differences among all study groups (LSD = 6.48). Diabetic patients with Pruritus had the highest RBS ($338 \pm 110 \text{ mg/dL}$), with significant differences compared to diabetic patients with acanthosis nigricans, bacterial infection, fungal infection, necrobiosis lipoidica and viral infection. On the other hand, this study found that the diabetics patients with nail changes had the highest mean of FBS ($170\pm17 \text{mg/dL}$) with significant

differences compared to diabetic patients with acanthosis nigricans, bacterial infection, diabetic foot, lichen planus and viral infection. Diabetic patients with Pruritus had the highest HbA1C (10.17 ± 2.9 %) with low significant difference (LSD = 1.36) compared to other study groups. Also, the present study showed that the diabetic patients with Pruritus had the highest values of both creatinine and blood urea (1.42 ± 0.5 mg/dL and 35.57 ± 15.12 mg/dL) with significant differences compared to all study groups (LSD = 0.3 and 12.3 for creatinine and blood urea, respectively).

Presenting disease	dis.dur	RBS mg/dL	FBS mg/dL	HbA1C	s.cretin mg/dL	bl urea mg/dL
bacterial infection	6.08a±3.10	237b±63	138b±28	8.08b±1.22	0.88b±0.12	14.08b±3.91
viral infection	5.80a±2.48	223b±40	139b±21	8.42b±1.38	0.93b±0.13	15.40b±3.74
fungal infection	6.75a±2.98	254b±58	154ab±26	8.80b±1.28	0.89b±0.14	14.90b±3.30
acanthosisnigricans	7.36a±4.45	249b±59	142b±20	8.82ab±0.9	0.94b±0.14	12.45b±4.39
acrochordon	6.88a±3.37	270ab±99	156ab±25	9.26ab±2.0	0.91b±0.11	12.66b±5.12
Pruritus	6.42a±4.82	338a±110	145ab±24	10.17a±2.9	1.42a±0.5	35.57a±15.12
diabetic bullae	9.50a±0.70	307ab±70	144ab±5	9.75ab±0.1	0.85b±0.07	14.00b±7.07
diabetic dermopathy	6.25a±3.30	278ab±20	152ab±22	8.57b±1.57	0.95b±0.12	14.25b±4.11
diabetic foot	5.40a±2.60	261ab±63	135b±27	8.08b±2.75	0.94b±0.15	15.40b±3.20
lichen planus	4.00a±4.82	243b±81	137b±37	7.75b±0.49	0.75b±0.07	11.50b±6.36
macular amyloidosis	7.50a±2.12	272ab±86	155ab±6	8.70b±0.42	0.85b±0.21	13.50b±6.12
nail changes	8.33a±3.26	285ab±31	170a±17	9.23ab±1.5	1.00b±0.12	17.33b±1.63
necrobiosislipoidica	6.50a±3.10	238b±59	156ab±27	9.35ab±1.4	0.85b±0.12	13.00b±3.82
Other skin disorders	6.53±3.24	255±65	146±26	8.67±1.57	0.93±0.22	15.50±7.82
LSD	6.48	72.12	26.5	1.36	0.3	12.3

	Table 3: Skin disorders in	diabetic patients and th	neir relationship with some	of biochemical parameters
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(P≤0.05)

According to mode of treatment, a significant differences were observed between types of skin disorders in diabetic patients who is taking the combination therapy (P. values 0.00), the highest percentage was 10(37.03%) in diabetic patients who suffering from bacterial infection, while other skin disorder (acrochordon, lichen planus and pruritus) were not reported in this group of diabetic patients. There is no a significant difference between diabetic patients who taking insulin therapy (P. value 0.092) and high value was 9 (23.68%)

in bacterial infection, while both macular amyloidosis and other skin disorders were not recorded in this group of patients with insulin therapy. On the other hand, those patients with oral hypoglycemic drugs showed high percentage of bacterial infection 15 (26.31%) whereas did not record any percentage of diabetic bullae, diabetic dermopathy and lichen planus. The results of statistical analysis showed a significant differences between diabetic patients and skin disorders (P. value 0.00). Table (4).

Table 4: The relationship between skin disorders in diabetic	patients with mode of treatment
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Presenting disease	N=122	Combination -n therapy	Insulin therapy	Oral hypoglycemics	P.value
acanthosisnigricans	11(9.1)	1(3.70%)	3 (7.89%)	7 (12.28%)	0.078
acrochordon	9(7.37)	0 (0%)	4(10.53%)	5 (8.77%)	0.439
bacterial infection	34(27.86)	10(37.03%)	9 (23.68%)	15(26.31%)	0.402
diabetic bullae	2(1.63)	1(3.70%)	1(2.63%)	0(0%)	1.00
diabetic dermopathy	4(3.27)	1(3.70%)	3(7.89%)	0(0%)	0.317
diabetic foot	5(4.09)	1(3.70%)	1(2.63%)	3(5.26%)	0.449
fungal infection	20(16.39)	6(24.44%)	5(13.16%)	9(15.79%)	0.522
lichen plannus	2(1.63)	0(0%)	2(5.26%)	0(0%)	0.00
macular amyloidosis	2(1.63)	1(3.70%)	0(0%)	1(1.75%)	1.00
nail changes	6(4.91)	1(3.70%)	4(10.53%)	1(1.75%)	0.223
necrobiosislipoidica	4(3.27)	2(7.41%)	1(2.63%)	1(1.75%)	0.779
Pruritus	7(5.73)	0(0%)	2(5.26%)	5(8.77%)	0.257
viral infection	10(8.19)	2(7.41%)	3(7.89%)	5(8.77%)	0.479
Others	6(4.91)	1(3.70%)	0(0%)	5(8.77%)	0.102
P. value	0.00	0.00	0.092	0.000	

DISCUSSION

The skin is the major border organ of human body, being the most exposed to environmental variations. However, it also

offers a window to what is going on inside the body so that changes to the skin may cause serious health problem, frequently serving as a marker for underlying internal disease (Franks, 2009; Rigopoulos *et al.*, 2011). Cutaneous manifestations of diabetes mellitus are considerably valuable to the clinician. They generally appear after the primary disease has developed but may appear coincidentally with its onset, or even precede diabetes by many years (Romano *et al.*, 1998). Upon four groups of skin disorders already described, most certified studies have shown the incidence of cutaneous complications connected with diabetes to be between 30 and 71%. (Romano *et al.*, 1998; Mahajan *et al.*, 2013).

The present study demonstrate that the skin disorders associated with diabetic patients had mean age 58.63 ± 9.42 , the duration of diabetes mellitus 6.73 ± 3.3 years, infection in mean levels of RBS was found (257.43 ± 75.77) mg/dl, FBS (147.79 ± 26.62) mg/dl, HbAlc% (8.76 ± 1.61) mg/dl.our study was confirm by Rahual and Prased (2017) in India who showed that the mean of age 51.22 ± 10.39 , duration of diabetes mellitus 7.14 ± 3.71 years, FBS (157.137 ± 44.48), HbAlc% (8.99 ± 1.05), also Niazet al. (2016) demonstrate that the mean duration of diabetes (8.5 ± 7), FBS (156 ± 50), RBS (213 ± 79), HbAlc%(8.6 ± 1.5).Altubouli and Ali (2019) in Libya who foundmean of age $54.4\pm9.4.39$, HBAlc (9.7 ± 1.6) but they found mean duration of diabetes 14.6 ± 6.6 years and this is different from our study.

Our results found the prevalence of skin disorders was relative similar 60(49.18%) and 62(50.81%) in males and females respectively, Niaz *et al.* (2016)have reported a higher frequency of skin disorders in females 59% and males 41%. On the other hand, Girisha and Viswanathan(2017) reported higher number of skin disorders in males more than females. The variation between percentage of infection in males and females may be due to size of study sample which is affect in this variation.

The current study showed that the cutaneous infections represented by bacterial, fungal and viral infection was most frequent while acanthosis nigricans and acrochordon was most repeatedly among noninfectious skin disorders. Our findings agreed with Ferringer & Miller (2002) who showed the cutaneous infections are most frequently in type 2 diabetic patients, and Niaz et al. (2016) demonstrate that higher number for skin disorders in diabetic patients was bacterial infection 26% followed by fungal infection 22%, acanthosis nigricans 20% and acrochordon 10%, while Girisha and Viswanathan (2017) exhibit that the fungal infection was most repeatedly between cutaneous infections 26.5% from bacterial and viral infection 6.75% and 2.75% respectively, and acanthosis nigricans was 5.5% less considerably from our study, as well the percentage of acrochordon was 17.75% higher than our results. The present study disagreed with results of Abdalla (2015) who mentioned that the xerosis was higher percentage 35% among diabetic patients. Yeung et al. (2018) indicated the ratio of xerosis was high 19.0% and acanthosis nigricanswas lower 0.9% when compared with our study.

Perhaps the reason for the increase in bacterial and fungal infections is due to the weak resistance of the diabetic patient, the occurrence of neuropathy and poor blood circulation as the patient loses the feeling of trauma and thus wounds that provide suitable habitats for microscopic organisms occur. Van Hattem *et al.* (2008) was supposed that poor

microcirculation and decreased immune response due to underlying microvascular and macrovascular complications of diabetic patients like peripheral vascular disease and peripheral neuropathy could render diabetes patients more vulnerable to infections. Also, Burke *et al.* (1999) elevated levels of insulin act on insulin-like growth factor receptors leading to the development of acanthosis nigricans. Crook (2000) demonstrate that acrochordon has been regarded as a sign of impaired glucose tolerance, Diabetes Mellitus, and increased cardiovascular (atherogenic lipid profile) risk.

Very few proportions of skin disorders uncommonly in diabetic patients were observed in current study such as granuloma annulare, perforating disorder, lichen planus, Rubeosis, vitiligo, xerosis and yellow skin and this findings was compatible to results Kataria et al. (2015) who recorded few percentages of cutaneous disorders uncommonly in diabetes mellitus such as lichen planus 1%, vitiligo 1%, psoriasis 1% and pemphigus vulgaris 1%, also Niaz et al. (2016) reported lower percentage in vitiligo 1%, lichen planus 0.5%, perforating dermatosis 1% and granuloma annulare 0.5%. James et al. (2011) showed that the yellow skin disease (Carotenodermia) is caused by increased levels of carotenoids may rarely occur in diabetic patients. Although the pathogenesis of lichen planus is not precisely known, but autoimmune reaction is the most possible reason (Bombeccari et al., 2011).

Diabetic foot is an important topic and our study recorded 4.09% in diabetic patients. The present study agrees with Rao *et al.* (2015) and Girisha and Viswanathan (2017) who mentioned the percentage of diabetic foot in diabetic patients 4%, while AL-Mutairi *et al.* (2006) recorded percentage 2% less than our study. Gkogkolou and Bohm (2014) showed several factors that contribute to the formation of diabetic foot including micro- and macro-angiopathy, neuropathy, skeletal deformities and wearing of unsuitable footwear.

When compared percentage of infection in present study between males and females of skin disorders in diabetic patients found the bacterial infection in males were higher than other skin disorders and fungal infection in females were most prevalent, on the other hand the other skin disorders was varied in their prevalence. Our study disagreed with results of Niaz et al. (2016) who reported that the bacterial infection in both males and females were 23% and 31% respectively while fungal infection was 22% for males and 23% for females, Also, Ahmed et al. (2009) refers to varied percentage regarding bacterial infection in the males 3.4% and females 15.7% whereas in fungal infection in males and females were detected 5% and 3.7% respectively. Niaz et al. (2016) showed very few proportions of other skin disorders such as lichen planus, perforating dermatosis and vitiligo in both gender. The reason in variation these percentages when compared with other studies may be due to the difference in size of study sample.

Our results demonstrate no significant differences among skin disorders in diabetic patients and duration of diabetes mellitus. However, the progression in the period of survival of the disease and level of uncontrolled blood glucose may be increase the risk of exposure to skin disorders. Through the increase in period of diabetes mellitus, non-enzymatic glycosylation of dermal collagen and mucopolysaccharides occurs which results in the different dermatological manifestations (Bhat *et al.*, 2006).

The present study found high values in levels of RBS, FBS and HBA1c when compared with normal values in other studies. Majeed *et al.* (2004) demonstrate that the normal range of HbA1c was taken as 5 – 7%. The statistical analysis showed significant differences in level of RBS between Pruritus and diabetic patients with acanthosis nigricans, bacterial infection, fungal infection, necrobiosis lipoidica and viral infection, also, nail changes was significantly highest mean of FBS when compared to diabetic patients with acanthosis nigricans, bacterial infection, bacterial infection, diabetic foot, lichen planus and viral infection.

The frequency of cutaneous complications with HbA1c level in present study showed that all the diabetic patients with these complications had uncontrolled diabetes. Pruritus had the highest HbA1c with low significant difference when compared to other skin disorders. Our findings emphasized by Majeed *et al.* (2004) who reported the diabetic patients with skin disorders had high HBA1c value. Poorana *et al.* (2019) found significant correlation between cutaneous infections and values of HbA1c in uncontrolled diabetes. Rahul and Prasad (2017) showed that the higher level of HbA1c in patients with diabetic bulla, scleredema, lichen planus and acanthosis nigricans while patients with psoriasis and vitiligo had statistically significant lower level of glycosylated hemoglobin.

The importance of studying RBS and FBS tests lies in diagnosis of patients with diabetes mellitus and determination level of sugar in the blood and its relationship to skin complications, also, HbAlc test determines the level of sugar in the blood during the last three months, Therefore, the high level of sugar in the blood leads to skin diseases as well as the low rate of nerve sensitivity which leads to weakness in blood circulation. World health organization (WHO) has endorsed the use of HbA1c as a screening test for persons at high risk of diabetes, and more importantly as a test for prediction of the risk of microvascular complications (Powers, 2008; WHO, 2011).

Our findings demonstrate that the percentage of diabetic patients with skin disorders who take oral hypoglycemic (46.72%) was higher than insulin therapy (31.14%) and combination therapy (21.31%). The present study showed a significant correlation between types of skin disorders in diabetic patients and both of oral hypoglycemic and combination therapy, mean while the skin disorders in diabetic patients who take insulin therapy were detected but there is no significant difference. Our results have already been confirmed by Ahmed et al. (2009) who reported the mode of treatment with oral hypoglycemic was higher 82.2%, than insulin 12.9% and combination therapy 4.9%. also our study agrees with study of Niaz et al. (2016) who mentioned the oral hypoglycemic 55%, insulin 23% and combination therapy 18%. Romano et al. (1998) showed that the cutaneous complications are classified into four groups, one of them is skin reactions to diabetic treatment (sulphonylureas or insulin). Van Hattem et al. (2008) and Rook & Burns (2010) mentioned the insulin injection may cause local and/or generalized allergic reactions which are attributed to

impurities in insulin preparations, preservatives, additives or the insulin molecule itself. Immediate local reaction, probably IgE mediated, starts with erythema and become urticarial and usually subsides in one hour. Ferringer & Miller (2002) demonstrate that the most cutaneous reactions to oral antidiabetic medications have been reported with first generation sulfonylureas, and 1 –5% of the patients taking sulfonylureas develop cutaneous reactions within two months of therapy, in the form of maculopapular drug rash. In conclusion, the present study was the first in Thi-Qar province that shows the skin complications associated with type 2 diabetes mellitus. Assured correlation between type 2 diabetes mellitus and cutaneous manifestation was observed in this study. Poor glycemic control is an important reason for the incidence of skin changes in diabetics. HbA1c level was high (>7) in diabetic patients with cutaneous complications. The current study recommends diabetic patients with health care and periodic examination to detect skin changes, especially the feet, for the purpose of treating them and avoiding their development. Give insulin injection correctly and not to repeat the same site.

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Cite this article: Ahmed Abdulhussein Kawen. 2020. Common Skin Disorders Associated with Type 2 Diabetes Mellitusin in Thi – Qar Province, Iraq. European Journal of Molecular & Clinical Medicine, 7(2), pp. 31 – 37, DOI: https://doi.org/10.31838/ejmcm.07.02.04