Cutaneous manifestations of diabetes mellitus

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One hundred fifty consecutive diabetes mellitus patients attending the endocrinology outpatient department and diabetic clinic constituted the study group. One hundred fifty age and sex matched non diabetics attending the medicine outpatient department were taken as controls. The majority, 65.3%, belonged to the 41-60 years age group; 56% were females, 97.3% had non-insulin dependent diabetes, 44.7% had duration of diabetes of 1-5 years. Among the study group, 66% had cutaneous manifestations as compared to 21.3% in the controls, which was statistically highly significant ($P < 0.0001$). Varied cutaneous manifestations were significantly seen in diabetics compared to controls ($P < 0.05$). Diabetic thick skin in the form of finger pebbles was the most common manifestation (49.49%), followed by fungal and bacterial infections (34.34%). The occurrence of cutaneous manifestations directly correlated with the duration of diabetes ($P < 0.05$). Majority of cases with cutaneous manifestations were having uncontrolled diabetes and had multiple and varied manifestations. As many as 87.8% of cases with cutaneous manifestations had various vascular complications.

KEY WORDS: Cutaneous manifestations, diabetes mellitus, glycosylated hemoglobin

Introduction

Diabetes mellitus (DM) is a worldwide problem and the most common endocrine disorder. Its prevalence is increasing in the present scenario of a sedentary lifestyle in the general population. Abnormalities of insulin and elevated blood glucose level lead to metabolic, vascular, neurological and immunological abnormalities. Affected organs include the cardiovascular, renal and nervous systems, eyes and the skin.[1] The skin is affected by both 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.[2] The association of certain skin diseases with DM has been fairly well recognized with an incidence rate ranging from 11.4[3] to 71%.[4]

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Methodology

One hundred fifty consecutive patients with diagnosis of DM attending the endocrinology outpatient department and diabetic clinic of department of medicine, Government Medical College, Jammu, constituted the subject material of present study (group A). One hundred fifty age and sex matched nondiabetic patients attending the medicine outpatient department constituted the control group (group B). Inclusion criteria for group A were raised fasting plasma glucose level as per the diagnostic criteria given by Ernesto;[5] those requiring treatment for their diabetes, both type 1 and type 2. Those with gestational diabetes were excluded. Patients with family history of diabetes and varicose veins were excluded from group B. A detailed history was elicited in each case, with particular reference to cutaneous complaints, including duration, history of evolution, progression and treatment modalities, if any. A detailed dermatological examination, general physical and systemic examination, including body-mass index, were carried out. Complete hemogram, fasting and postprandial blood sugar, urine examination, renal and liver function tests, lipid profile, 24 hours' urinary protein, fundus examination and electrocardiogram were done in each patient. Control of diabetes was assessed by glycosylated hemoglobin (HbA_{1c}) estimation (controlled 4.5% to 7.0%; and uncontrolled ≥ 7%). Relevant

microbiological and histopathological investigations to confirm the diagnosis were carried out.

Results

Among the 150 diabetic cases, there were 84 (56%) females and 66 (44%) males; the male-female ratio was 1:1.27. The age of patients ranged from 10 to 80 years (mean 50.28 ± 11.80 years), and the most common age groups were 41-50 (33.3%), 51-60 (32%), 31-40 (18.6%). The majority (97.7%) of patients had type 2 DM; only 2.3% had type 1 DM. Of the diabetic patients, 66% had one or more associated cutaneous manifestations. On the other hand, among the age and sex matched controls, only 21.3% had cutaneous manifestations. The cutaneous manifestations were thus positively associated with diabetes; this was statistically highly significant ($P < 0.0001$). The cutaneous manifestations were more prevalent in 41-50 years age group (34.3%), followed by 51-60 years (30.3%) and 31-40 years (18.15%) age groups. Female patients had higher incidence (55.6%) as compared to male diabetics. Cutaneous manifestations were more prevalent in overweight and obese diabetics. The duration of diabetes ranged from 10 days to 22 years (mean 4.78 ± 4.69 years). In diabetic patients with cutaneous manifestations, majority (37.37%) had 1-5 years of duration of diabetes, followed by 6-10 years (24.24%), <1 year (23.73%) and >10 years (15.15%). When comparing this with diabetes without cutaneous manifestations, the difference was statistically significant. The various cutaneous manifestations observed in the present study as per the classification of Ferringer and Miller[6] are delineated in Table 1.

Diabetic thick skin in the form of finger pebbles constituted the largest group, affecting 49 (49.49%) patients. Cutaneous infections constituted the second commonest manifestation (34.34%), as delineated in Table 2.

Among the cutaneous disorders strongly associated with diabetes, 17 patients had diabetic dermopathy, 2 had rubeosis facie, 2 had necrobiosis lipoidica, 4 had bullosis diabeticorum, 4 had xanthelasma. Skin tags were seen in 17 and acanthosis nigricans in 8 patients. Pruritus was seen in 12 patients. Eight patients had dermatosis, which are known to be associated with an increased incidence of diabetes. Oral lichen planus (LP) was seen in 4 patients, vitiligo in 2, psoriasis and pigmented purpuric dermatosis each in 1 patient. Cutaneous manifestations of diabetic complications included loss of hair in the legs in 17, nail changes in 16 and diabetic foot in 4 patients. Two patients had reactions to oral hypoglycemic drugs, and 3 had reactions to insulin in the form of pruritic erythema in 1 and injection site pigmentation in 2 patients. Cherry angiomas were seen in 14, xerosis in 5 and macular amyloidosis in 4 patients.

Table 2: Cutaneous infections in diabetics

Infections	No	Percentage
Bacterial	14	14.14
Candidal	10	10.10
Dermatophytic	8	8.8
Viral	2	2.2

Relation with glycemic control

Out of 99 patients with cutaneous manifestations, 55.56% had uncontrolled and 44.44% had controlled glycosylated hemoglobin (HbA_{1c}) levels.

Association with other diabetic complications

Table 3 delineates the systemic complications of DM in patients with and without cutaneous manifestations. Hypertension was seen in a higher percentage of diabetics with cutaneous manifestations (46.46%) than in those without such manifestations (17.64%). Likewise coronary artery disease, PVD, nephropathy and retinopathy were seen in a higher percentage of diabetics with cutaneous manifestations, i.e., 12.12% *vs.* 5.88%, 4.04% *vs.* 1.96%, 11.11% *vs.* 0% and 10.10% *vs.* 3.92% in controls respectively. Peripheral neuropathy was more common in patients without cutaneous manifestations (7.84%) than in those with skin manifestations (4.04%).

Table 1: Cutaneous manifestations of diabetes mellitus in 99 patients

Cutaneous manifestations	No	Percentage
Cutaneous disorders associated with diabetes	49	49.9
Cutaneous infections	34	34.34
Pruritus	12	12.12
Cutaneous disorders weakly associated with diabetes	8	8.8
Cutaneous manifestations of diabetic complications	17	17.17
Cutaneous reactions to diabetic treatment	5	5.5
Miscellaneous	20	20.20

Table 3: Systemic complications in diabetic patients

Complications	Cutaneous manifestations				Total
	Present (n =99)		Absent (n =51)		
	No.	%	No.	%	
Hypertension	46	46.46	9	17.64	55
Coronary artery disease	12	12.12	3	5.88	15
PVD	4	4.04	1	1.96	5
Nephropathy	11	11.11	0	0	11
Retinopathy	10	10.10	2	3.92	12
Neuropathy	4	4.04	4	7.84	8

Statistically significant association was seen with hypertension (P = 0.0005) and nephropathy (P = 0.03).

Cutaneous manifestations in group B

Thirty-two (21.3%) patients out of 150 age- and sex-matched controls had cutaneous lesions. Finger pebbles formed the largest group (28.12% of patients), followed by infections (24.98% of patients), cherry angiomas in 5 (15.6%), skin tags in 4 (12.65%) patients. Two patients (6.25%) each had acanthosis nigricans, xanthelasma, and one patient each had vitiligo, pruritis and macular amyloidosis.

Discussion

In the present study, some form of cutaneous involvement was present in 66% in group A and 21.3% in group B, which was statistically highly significant. Braverman[7] found cutaneous manifestations in 30% of patients, whereas Romano *et al.*,[8] Nigam and Pande,[9] Mahajan *et al.*,[2] Yosipovitch *et al.*,[4] Wahid and Kanjee[10] found these in 60, 61, 64, 71 and 82% respectively. The frequency of patients with cutaneous manifestations in the fourth, fifth and sixth decade was 18.1, 34.3 and 30.3% respectively. Similar frequency was reported by Romano *et al.*,[8] whereas Nigam and Pande[9] reported higher frequency. Our study showed female predominance, as was reported by Mahajan *et al.*,[2] and Lugo Somolinos *et al.*,[11] The correlation of cutaneous manifestations with obesity status showed statistically significant difference (P< 0.05), as was reported by Yosipovitch *et al.*,[4] In majority of diabetics, the duration of disease was less than 6 years. The incidence of cutaneous manifestation was significantly correlated with the duration of diabetes (P < 0.05). Similar association has been reported by Alteras and Saryt[12] and Dogra *et al.*,[13] As the duration of diabetes increases, there is non-enzymatic glycosylation of dermal collagen and mucopolysaccharides, leading to various cutaneous manifestations. Although cutaneous reactions to medication were seen in only 5 patients, other skin findings were more frequent in patients on oral hypoglycemics than on insulin, which may be due to their poor metabolic control.

Majority of the patients with skin lesions had uncontrolled diabetes, as was found by Yosipovitch *et al.*,[4] and Sawhney *et al.*,[14] Uncontrolled diabetes increases the risk of development of microangiopathy and related complications or sequelae. Our study showed that a higher percentage (87.87%) of patients with cutaneous manifestations had systemic complications like hypertension, coronary artery disease, peripheral vascular disease, nephropathy, retinopathy and peripheral neuropathy as compared to diabetic patients without cutaneous manifestations (37.24%). Similar values of 89 and 55.5% were reported by Mahajan *et al.*,[2] and Shemer *et al.*,[15] respectively. Hence the cutaneous manifestations correlate with systemic manifestations of diabetes.

From the foregoing account, we conclude that the skin is involved in diabetes quite often and whenever patients present with multiple skin manifestations, their diabetic status should be checked and controlled; or if they are obese, a high index of suspicion should be kept regarding their diabetic status. The recognition of these findings is the key to treatment and prevention.

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Source of Support: Nil, **Conflict of Interest:** None declared.