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Original Article

Cutaneous manifestations in patients with type 2 diabetes mellitus and normal controls

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ABSTRACT

Objectives: The objectives of the study were (1) to study the cutaneous manifestations in patients with type 2 diabetes mellitus (DM) in comparison to normal subjects and (2) to document the association between cutaneous manifestations and complications of DM.

Materials and Methods: In this 1-year comparative cross-sectional study, 100 patients receiving treatment at the diabetic clinic of a tertiary center were evaluated for cutaneous manifestations and complications due to diabetes. The cutaneous features in diabetics were compared with that of normal controls. An attempt was made to find out any association between cutaneous features of DM and internal organ involvement due to diabetes.

Results: Cutaneous manifestations were more frequent in patients with type 2 DM than normal controls. The most common manifestation in diabetics was fungal infection followed by bacterial infection. Diabetic dermopathy was found to have statistically significant association with nephropathy, retinopathy, and neuropathy due to type 2 DM.

Limitations: Limited sample size and study confined to a tertiary referral center.

Conclusions: Dermatology manifestations provide important clues of prognostic significance in type 2 DM.

Keywords: Type 2 diabetes mellitus, Cutaneous manifestations, Internal organ involvement, Diabetic bulla, Diabetic dermopathy

INTRODUCTION

Diabetes mellitus (DM) is a common endocrinopathy and assumes significance for its ability to adversely affect the various internal organs. It can also derail the immune system of the affected. Hence, it is not surprising for diabetes to affect skin (the largest organ) producing different lesions. At times, evaluation for skin lesions leads to diagnosis of underlying diabetes. In a known diabetic, skin changes may provide warning signals regarding systemic involvement.

In this study, we have attempted to record the cutaneous manifestations of type 2 DM and its association with organ involvement.

MATERIALS AND METHODS

After obtaining clearance from the Institutional Ethics Committee and receiving written informed consent from individual study subject, patients with type 2 DM (on therapy or freshly diagnosed cases)

and equal number of age- and sex-matched controls without DM (as confirmed by blood investigations) were included in this comparative cross-sectional study. The sample size was determined as minimum of 84 patients based on previous years' statistics. Patients were selected from the diabetic clinic of our institution. Controls (who do not have diabetes confirmed by blood investigations) were selected from the bystanders of patients attending the dermatology OPD of our center.

The study period was 1 year from January 01, 2015 to December 31, 2015.

Inclusion criteria

Patients diagnosed to have DM after the age of 30 years, including known cases of type 2 DM already on treatment or newly detected diabetic patients, based on the American Diabetic Association criteria (symptoms of diabetes and random plasma sugar >200 mg/dl or fasting plasma sugar >126 mg/dl or >200 mg/dl 2 h after 75 g oral glucose or hemoglobin A1c >6.5%) were included in this study.[1]

Exclusion criteria

Patients with known comorbid conditions requiring long-term steroid therapy and patients suffering from immunocompromised conditions, type 1 DM, pulmonary tuberculosis, collagen vascular diseases, thyroid disorders, and primary dermatological conditions were excluded from the study.

Using a preset proforma, information on demography and evolution of skin manifestations were collected from each subject, including the treatment received.

A thorough clinical examination was carried out to document the mucocutaneous lesions in natural light with special reference to infections, xanthoma, acanthosis nigricans, necrobiosis lipoidica, rubeosis, dermopathy, diabetic bulla, gangrene, trophic ulcer, sensory neuropathy, lipodystrophy, finger pebbles, skin tag, scleredema diabeticorum, granuloma annulare, perforating disorder, earlobe crease, and limited joint mobility in cases and controls. Blood sugar level was determined on venous samples. Urine microscopy, renal function tests, fasting lipid profile, electrocardiogram, 24 h urine protein estimation, and fundoscopy were performed wherever indicated. Histopathology and microbiology analyses were carried out wherever necessary to confirm the diagnosis.

The data were entered in Microsoft Excel and comparison between cases and controls was done using Pearson Chi-square test ($P < 0.05$ was considered as significant).

RESULTS

The study group comprised 100 known type 2 DM patients above 30 years of age who attended the diabetic clinic and 100 age- and sex-matched controls who were drawn from the bystanders of patients attending dermatology outpatient clinic of our center.

The age of the study group ranged from 34 to 76 years [Figure 1]. The majority of patients were between 50 and 59 years (39, 39%). The least number of patients belonged to the 30–39 years group (6, 6%).

There were 47 males and 53 females among the cases.

Hypertension was observed in 45 (45%) cases and in nine (9%) controls ($P < 0.001$). Fourteen (14%) patients and one (1%) control had atherosclerotic heart disease ($P < 0.001$). The difference was statistically significant with $P < 0.001$ for both.

Of 100 patients, 88 (88%) had cutaneous manifestations [Table 1], whereas 28 (28%) controls had skin lesions. This was statistically significant ($P < 0.001$).

The majority of patients had disease duration of 10–14 years (39, 39%). Two patients (2%) were recently detected diabetics with duration of disease below 1 year. Three patients (3%) had disease duration of more than 25 years [Figure 2].

Ten (10%) patients had diabetic nephropathy and 11 (11%) had diabetic retinopathy. None of the controls had nephropathy or retinopathy.

Peripheral neuropathy was present in 25 of 100 diabetic patients and 1 of 100 controls. The frequency in diabetics was statistically significant ($P < 0.001$). 9/25 and 8/25 patients with peripheral neuropathy had diabetic retinopathy and nephropathy, respectively, and the association was statistically significant ($P < 0.001$) for both.

All patients with duration of diabetes more than 15 years were found to have cutaneous lesions (27/27, 100%), whereas 61 of 73 patients (83.6%) with duration <15 years had cutaneous lesions ($P = 0.03$).

Among the 100 patients, diabetic status was well controlled in 34 (34%), whereas 66 (66%) had uncontrolled DM. 64/66 (97%) patients with uncontrolled diabetes and 24/34 (70.6%) with

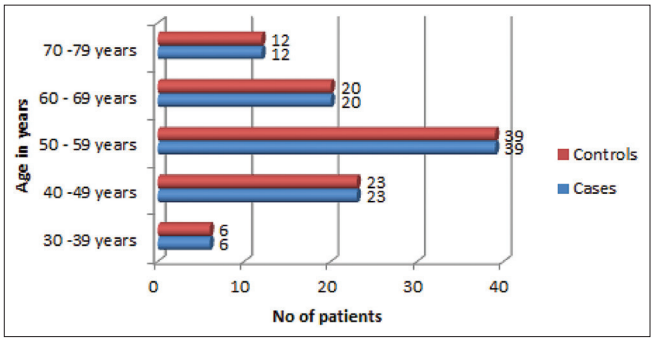

Figure 1: Age distribution of study population.

controlled diabetic status had cutaneous manifestations and the disparity was significant statistically ($P < 0.001$).

Cutaneous manifestations were the initial presentation of DM in 15 (15%) patients, and 10/15 had recurrent bacterial infections and the rest had candidiasis.

16/36 (44.4%) patients who developed bacterial infections suffered from secondary infections and the rest had primary pyodermas (20/36, 55.5%). The two controls who documented bacterial infections had furuncle and secondary infection of traumatic injury, respectively. The disparity noted was statistically significant ($P < 0.001$).

Table 1: Pattern of cutaneous manifestations in type 2 diabetes mellitus cases and controls.

Cutaneous manifestation	Cases %	Controls %
Bacterial infections	36	2
Fungal infections	55	10
Viral infections	11	5
Dermopathy	16	0
Diabetic bullae	3	0
Necrobiosis lipoidica	1	0
Peripheral neuropathy	25	1
Trophic ulcer	2	0
Wet gangrene	2	0
Skin tag	27	6
Acanthosis nigricans	13	2
Xanthelasma	5	1
Hirsutism	1	0
Scleredema diabeticorum	1	0
Granuloma annulare	1	0
Xerosis	21	6
Edema	13	0
Diagonal ear lobe crease	10	1
Perforating collagenosis	2	0
Insulin lipodystrophy	1	0
Lichenoid reaction to oral hypoglycemic agents	1	0

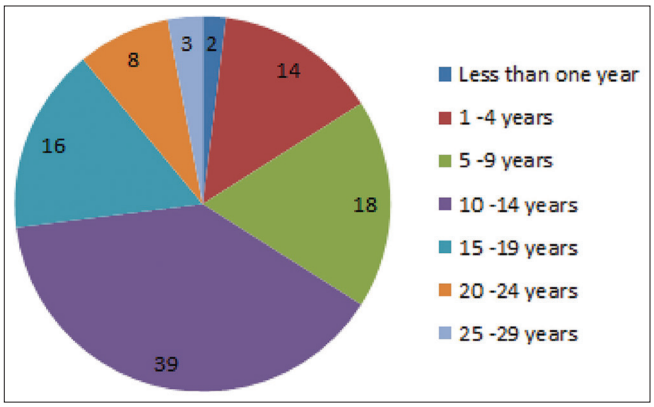

Figure 2: Distribution of patients based on duration of type 2 diabetes mellitus.

Among cases manifesting fungal infections, candidiasis predominated, (32/55, 58.2%) followed by onychomycosis (9/55, 16.4%), dermatophytosis, (8/55, 14.5%) and tinea versicolor (6/55, 10.9%). Among the ten controls who had fungal infections, 4 (40%) had candidiasis, 3 (30%) tinea versicolor, 2 (20%) onychomycosis, and 1 (10%) had dermatophytosis. The difference in frequency of fungal infections between cases and controls was significant ($P < 0.001$).

Verruca vulgaris was seen in 10% (10/100) of diabetic patients and 5% (5/100) of controls. The difference was not statistically significant ($P = 0.239$). One patient had herpes zoster.

Sixteen (16%) patients had diabetic dermopathy [Figure 3] which was statistically significant ($P < 0.001$). Of the total 16 patients with dermopathy, 14 (87.5%) had more than 15 years duration of type 2 diabetes which was statistically significant ($P < 0.001$). The remaining two (12.5%) had disease duration of more than 10 years. None of the 34 patients with disease duration of <10 years had diabetic dermopathy.

All the 10 diabetic nephropathy and the 11 diabetic retinopathy cases manifested dermopathy. Six patients without nephropathy and five without retinopathy had dermopathy. The association of dermopathy with nephropathy and retinopathy was found to be statistically significant ($P < 0.001$) for both.

Diabetic bullae [Figure 4] were seen in three (3%) cases and none of the controls. This was not found to be statistically significant. All these patients had diabetic retinopathy and nephropathy. Two patients with diabetic bullae had peripheral neuropathy. The association was statistically significant for diabetic retinopathy and nephropathy ($P < 0.001$) but not significant for neuropathy.

Necrobiosis lipoidica diabeticorum [Figure 5] was found in one patient and in none of the controls. The patient who was

Figure 3: Diabetic dermopathy.

Figure 4: Diabetic bulla.

Figure 5: Necrobiosis lipoidica diabeticorum.

a female had ulcerated lesion. She was also suffering from coronary artery disease.

Wet gangrene was seen two patients. None of the controls had it. The difference was found to be statistically not significant.

Of the 100 patients, 27 (27%) had skin tags, 19 (19%) acanthosis nigricans, five (5%) xanthelasma, and one (1%) had hirsutism. Among the controls, six (6%) had skin tag, two (2%) had acanthosis nigricans, and one (1%) had xanthelasma.

The prevalence of these lesions in diabetic patients was significant statistically for skin tag and acanthosis nigricans ($P < 0.001$) for both.

Diagonal ear lobe crease was noted in 10 patients (10%) and one control (1%). $P = 0.01$. 6/10 (60%) cases with diagonal ear lobe crease manifested coronary artery disease, while 8/90 patients who did not have the finding had coronary artery disease ($P < 0.001$). Four (40%) patients with diagonal ear lobe crease had diabetic retinopathy and 7/90 patients without diagonal ear lobe crease manifested the latter ($P = 0.012$).

The other manifestations documented in study subjects did not show any statistically significant association with DM.

One of the 100 cases (1%) (who also suffered from diabetic nephropathy and retinopathy) manifested insulin induced lipodystrophy. Another patient developed oral lichenoid reaction to sulfonylurea which was replaced with biguanide.

DISCUSSION

The maximum number of patients belonging to the 50–59-year group (39%) was as expected in the patient profile suffering from type 2 DM seeking treatment in a tertiary center. Age of onset of type 2 DM is usually in the forties and those with long-standing disease are more likely to suffer from disease-associated organ damage warranting care from the specialty clinic of a tertiary referral center. This was supported by our observation of 66% of the study participants having disease duration of more than 15 years.

Only 6% of patients being below 40 years was discordant to the observation of Song and Hardisty, who documented a prevalence of 24% in those below 40 years.[2] This disparity in our study could be due to patients with early disease without major organ damage preferring to seek treatment from nearby centers.

The observation of uncontrolled DM in 66% of the study population was consistent with literature.[3] The frequency of cutaneous manifestations recorded in the current study was similar to certain earlier studies but was higher than the 63% reported by Foss *et al*.[4-7]

The greater percentage of patients with uncontrolled disease manifesting cutaneous lesions in comparison to those with controlled glycemic status (97% and 70.6%, respectively) was as reported in literature.[2]

Predominant manifestations in the study group being fungal infections followed by bacterial infections were concordant to existing literature.[5,6]

Cutaneous manifestation being the presenting symptom of DM in 15% of patients as observed by us was consistent with the findings of others.[8-11]

Higher frequency of skin manifestations documented in patients with a longer duration of DM as noted by us was consistent with the findings of Goyal *et al*. and Mahajan *et al*.[12,13]

Our observation of diabetic dermopathy in 16% of cases was comparable to certain previous studies, but others have reported higher prevalence.[3,14] The reason for the low frequency of diabetic dermopathy in one previous Indian study (which was similar to ours) was attributed to the possibility of the same being overlooked in dark skin of Indians.[3]

Our observation of dermopathy being an indicator of complications of diabetes such as nephropathy, retinopathy, and neuropathy was consistent with the findings of previous authors.[3,14] We suggest that all those with diabetic dermopathy need to be screened for complications of DM.

The lack of a significant association between diabetic bulla and peripheral neuropathy in this study was contrary to previous observations.[15] This could be attributed to the rarity of the manifestation in the study participants.

The 1% of frequency observed for necrobiosis lipoidica diabeticorum by us was consistent with previous reports.[16] Ulceration of necrobiosis lipoidica diabeticorum as observed by us was reported in 35% of patients by Lowitt and Dover.[16] The comorbidity of coronary artery disease documented in our patient with necrobiosis lipoidica diabeticorum was concordant with the previous report of 50% of patients with this cutaneous manifestation of DM having coexisting end-organ damage.

The statistically significant association noted between diagonal ear lobe crease and coronary artery disease and the former with diabetic retinopathy was reported earlier.[17,18]

The adverse reactions documented in the study group to hypoglycemia agents were reported by others.[19,20]

Limitations

The study carried out in a tertiary care center is likely to miss the cutaneous manifestations of DM in general population. The rare manifestations of diabetes like necrobiosis lipoidica diabeticorum could not be well studied with the limited sample size of hundred.

Despite these limitations, we were able to document the common cutaneous features of type 2 DM and the importance of diabetic dermopathy, diabetic bullae, and diagonal ear lobe crease as markers of internal organ damage.

CONCLUSIONS

Skin manifestations can be the presenting sign of type 2 DM or they can indicate underlying diabetes-induced organ damage in known diabetics. Thorough dermatology evaluation can provide valuable clues in diagnosing as well as defining prognosis of type 2 DM.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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