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Prevalence of skin changes in diabetes mellitus and its correlation with internal diseases: A single center observational study

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Abstract
Introduction: This single-center observational cross-sectional study has been done in an attempt to find out the prevalence of various skin manifestations in diabetes patients (DM) and their correlation with diabetes control and complications.
Materials and Methods: Skin manifestations present over 12 months among those attend diabetes clinic were included in the study. Apart from demographic data and type, patients were also screened for micro vascular complications and control of diabetes over last 3 months.
Results and Discussion: Sixty (n = 60) diabetes patisents (Type 1 DM, 9 patients and Type 2 DM 51 patients) have been found to have various skin lesions. Thirty-one (51.67%) patients presented with infectious conditions, vascular complications were present in 21 (35%) and dermatomes belonging to the miscellaneous group were present in 50 (83.33%) patients.
Pyoderma, diabetic dermopathy, and pruritus without skin lesions were found to be most common manifestations in infective, vascular and miscellaneous group, respectively. Higher level of HB1AC was found in patient with diabetic bulla (10.5 ± 0), scleredema (9.75 ± 0.77), lichen planus (9.3 ± 1.6), and acanthosis nigricans (9.15 ± 0.89). Patients with psoriasis and vitiligo had statistically significant lower level of glycosylated hemoglobin (P =< 0.001 and 0.03, respectively). However, no association of any kind of skin manifestation with DM with other microangiopathic complications was found in this study.

Keywords: diabetes mellitus, micro vascular complications, observational study, skin manifestations

1. Introduction
Diabetes mellitus (DM) is a metabolic disease characterized by relative or absolute insulin deficiency. The metabolic abnormality in DM results in gross defect in protein, carbohydrate and fat metabolism [1]. Presently DM affects individuals of all ages and in all socio-economic segments of the population. The International Diabetes Federation (IDF) estimated the total number of diabetic subjects to be around 40.9 million in India and this is further set to raise to 69.9 million by the year 2025 [2].
WHO suggests that the number of diabetic subjects would increase to 80 million by the year 2030 in India [3]. Skin lesions are frequently observed in diabetic patients and about 30% of diabetics have cutaneous disorders [4].
There are many proposed patho-mechanism for skin involvement in DM, which includes abnormal carbohydrate metabolism, other altered metabolic pathways, atherosclerosis, microangiopathy, neuron degeneration and impaired host immune mechanism [5]. Some studies revealed the correlation of skin manifestation of DM with microangiopathic complications [6, 7]. However, a large-scale study in Indian population aiming at finding out the correlation of the skin manifestations with internal complication of DM is lacking till date.
There is also paucity of studies in this Eastern India to find out the prevalence of various types of skin changes among the diabetic individuals; hence, this study is an attempt to fill this lacunae. Moreover, this study also aims at searching the relationship of skin changes with microangiopathic complications of DM, so as to use them as early marker of the internal complications.

2. Materials and Methods
All patients attending the Diabetes clinic of the institute (held twice a week) were evaluated for the presence of any skin lesion over a period of 12 months. Diabetes was diagnosed as per the criteria laid down by National Diabetes Data Group and World Health Organization, if any two of the following criteria were present: Symptom of DM and random plasma glucose ≥200 mg/dl or fasting blood sugar (8 hours) ≥126 mg/dl or 2 hours plasma glucose (75 mg) ≥200 mg/dl during an oral glucose tolerance test [8].
Detail evaluation of demographic profile and clinical manifestations were carried out. Emphasis was given to assess the micro vascular complications (i.e. nephropathy, neuropathy, and retinopathy) and relevant investigations were done. Neuropathy was diagnosed by nerve conduction velocity test (NCV) and criteria detailed by Foster [9].
Nephropathy was diagnosed if microalbuminuria is present excluding other contributing factors. Assessment of diabetic retinopathy was done by opinion of ophthalmologist. The glycemic control was evaluated by measuring the glycosylated hemoglobin (Hb1AC).
For the purpose of the study we had divided the skin manifestations due to DM in three different categories:
Cutaneous infections due to immune alterations like bacterial, viral and fungal infections symptoms due to vascular abnormalities and miscellaneous conditions, where etio-pathogenesis could not be explained by vascular or infective complications. Data were statistically described in terms of range, median, mean ± standard deviation (±SD), as appropriate. The continuous variable data were analyzed using the t-test and the categorical data were analyzed using the

Chi-square test. Medcalc statistical software® version 9.6.4.0 (http:// www.medcalc.be) was used for statistical analysis and a $P \leq 0.05$ was considered statistically significant.

3. Results

Among 200 patients who attended the diabetes clinic over the 6 month period, 60 patients (9 of them had type 1 DM and 51 had type 2 DM) had skin changes. Demographic profiles of the patients are represented in Table 1. The mean age and BMI were significantly high in the Type 2 DM compared to Type 1 DM ($P < 0.001$ and $P = 0.002$, respectively).

We found no significant gender difference or significant difference in blood sugar level or glycosylated hemoglobin (Hb1AC) among Type 1 and Type 2 DM patients. Thirty-one (51.67%) patients presented with infectious conditions, vascular complications were present in 21 (35%) and dermatomes belonging to the miscellaneous group as per our study protocol were present in 50 (83.33%) patients. Among the infectious complications pyoderma was the most common complication (n = 14, 23%), followed by onychomycosis and genital candidiasis (n = 4, 6.67% each) being most common among the infectious complications.

Table 1: Demographic profile of study population

Clinico-demographic parameters	Type 1 DM (*N*=9)	Type 2 DM (*N*=51)	*P*
Age			
Mean±SD	34.56±18.25	51.22±10.39	0.0002
Range (median)	20.53 to 48.58 (36)	7.14±3.71	
Sex (Male: Female)	4;5	30:21	0.6616
Duration of DM	7.44±3.64	7.14±3.71	0.8195
Range (median)	4.64 to 10.24 (7)	6.09 to 8.18 (7)	
FBS			
Mean±SD	153±32.14	157.137±44.484	0.7911
Range (median)	128.2978 to 177.7022 (136)	144.6258 to 169.6488 (137)	
PPBS			
Mean±SD	253.8889±71.4850	247.8235±50.5754	0.5334
Range (median)	198.9406 to 308.8372 (220)	233.5990 to 262.0481 (235)	
HBA1c			
Mean±SD	8.7222±1.4342	8.998±1.0569	1.0569
Range (median)	7.0311 to 10.6845 (8.6)	8.7008 to 9.2953 (9.2)	
BMI			
Mean±SD	19.5889±5.3790	25.0078±4.5161	0.0021*
Range (median)	15.4542 to 23.7236 (17.4)	23.7377 to 26.2780 (25.5)	
Retinopathy (present: Absent)	1:8	13:38	0.6080
Nephropathy (present: Absent)	1:8	13:38	0.6080

Regarding age at presentation, wet gangrene (32.5 ± 7.77 years), pruritus (35.37 ± 16.61 years) and ichthysis and xerosis (38 ± 48.08 years) were found to arise at an early age in our study population. Genital candidiasis (62.25 ± 2.21 years) and onychomycosis (64 ± 6.73 years) were found to be significantly associated with those patients presenting at advancing age ($P = 0.0357$ and $P = 0.0147$, respectively).

Higher level of HB1AC was found in patient with diabetic bulla (10.5 ± 0), scleredema (9.75 ± 0.77), lichen planus (9.3 ± 1.6), acanthosis nigricans (9.15 ± 0.89). Patients with psoriasis and vitiligo had statistically significant lower level of glycosylated hemoglobin ($P =< 0.001$ and 0.03, respectively). Table 2 represents relationship of microangiopathic complications of DM (retinopathy, nephropathy and neuropathy) with skin changes. No statistically significant associations of any of the cutaneous manifestations with DM control were found.

Discussion

DM is a common condition. International Diabetes Federation (IDF) estimated the total number of diabetic subjects to be around 40.9 million in India and this is further set to raise to 69.9 million by the year 2025 [2]. Almost all diabetic patients eventually develop skin complications. Most of the time a patient is unaware that his skin condition is due to diabetes. So the exact data of prevalence of skin changes among the diabetic patients is difficult to obtain.

Various studies reported 7.6% to 30% [4, 10, 11] study carried out by Yosipovitch *et al.* found prevalence of skin manifestations among the Type 1 DM population is as high as 71% [12] In our study a wide variation of prevalence of skin changes of diabetic population may be due to lack of knowledge and attitude of the diabetic patients towards their skin problem.

In fact, an institution-based cross-sectional study in this eastern part of the world carried out by Hussain *et al.* [13] found that in most of the cases the person is not concern that their skin condition is due to DM and even in more than in 50% of the treating physician fails to inform the complications. Various study reported age of presentation of Type 2 DM patients with skin manifestation is between 5th to 6th decade [10, 13, 14]. Age of presentation of Type 2 DM of our study populations is 51.21 ± 10.38 which matches with previous study findings.

Among the patients presented with skin manifestations 15% was Type 1 and 85% Type 2 DM. Study carried out by Cvitanovi *et al.* [11] had almost similar finding. The occurrence of lower incidence of skin changes among type 1 DM might be due to lower disease burden of Type 1 DM patients as compared to Type 2 DM patients. The prevalence of different types of skin changes varies considerably in different studies. A south Indian study revealed that infectious complications are

most common complications. Fungal infection was the most common infectious complication.

Among the other complications, 2(2.27%) had xanthelasma palpebrarum, 1(1.14%) had pruritus without any skin lesions, 2 patients had diabetic dermopaty and 1(1.14%) had diabetic bulla. Polyneuropathy and diabetic ulcer was noted in one patient each. Miscellaneous conditions like vitiligo, lichen planus, drug reactions, lichen simplex, pustular bacterid, atopic dermatitis, eczema, psoriasis, skin tag and pemphigus vulgaris were noted in 20 patients altogether. Pruritus was the most common skin symptom [10].

Another Indian Study carrier out by Mahajan *et al.* [15] in North India found infectious complication was most common. On the other hand, a Croatian-based study showed diabetic dermopathy was the most common cutaneous manifestation (32, 14%). The second common was skin infections associated with DM and were found in 16.47% patient which is much lower than Eastern studies.

Third group represented diabetic complications, and was found in 11 patients (13, 10%) and the most common changes were ulcers in 4(4, 76%) patients and xerosis in 4(4, 76%) patients [11]. Another western study among the populations of Type 1 DM reported xerosis as the most common skin manifestation. That study found that ichthyosiform skin changes of the shins, scleroderma-like skin changes, tinea pedis, and dry scaly palms were detected in 48 vs. 7%, 39 vs. 0%, 32 vs. 7%, and 21 vs. 0.8% of the patients and control subjects, respectively [12].

Considering individual types infectious complications are the most common complication in our study which matches the findings of the other studies of this eastern part of the world. However, our study found pyoderma as the most common cutaneous manifestation, while other study found mycosis as the most common skin findings. Our study also revealed statistically significantly higher occurrence of onychomycosis and genital candidiasis among the diabetic populations with increasing age.

Diabetic dermopathic was found to be the most common microangiopathic cutaneous complication. We also found statistically significant lower level of Hb 1Ac among the patients with vitiligo and psoriasis. This may be due to patients with psoriasis and vitiligo becomes more stringent regarding their diabetic control.

Table 2: Relation of various skin diseases with micro vascular complications

	Retinopathy (present/absent)	*P* value	Neuropathy (present/absent)	*P* value	Nephropathy (present/absent)	*P* value
Porokeratosis (*n*=2)	001/001	0.9153	000/002	1	001/001	0.9548
Acanthosis nigricans (*n*=7)	001/006	0.6662	001/006	0.8164	003/004	0.4099
Dermopathy (*n*=13)	002/011	0.4106	005/007	0.3657	005/007	0.3012
Diabetic bullae (*n*=1)	000/001	0.6278	001/000	0.5604	001/000	0.5604
Diabetic foot	001/005	0.8485	002/004	1	000/006	0.3598
Genital candidiasis	000/004	0.467	001/003	0.5501	001/003	0.5501
Ichthyosis and xerosis	002/000	0.1363	001/001	1	001/001	0.9548
Intertrigo	001/001	0.6455	000/003	0.7324	000/003	0.7794
Lichen planus	001/002	0.9153	000/002	0.9548	000/002	0.9548
Limited joint mobility	001/001	0.9153	001/001	1	000/002	0.9548
Maculopapular rash	000/004	0.467	001/003	0.5501	001/003	0.5959
Onychomycosis	003/001	0.1165	002/002	0.5501	002/002	0.4881
PPD	001/003	0.6737	001/003	0.5501	001/003	0.5959
Pruritus	003/005	0.8441	001/007	0.661	002/006	0.742
Psoriasis	000/002	0.9153	000/002	1	000/002	0.9548
Pyoderma	005/009	0.7179	003/011	1	000/014	0.0459
Scleredema	000/002	0.9153	000/002	1	001/001	0.9548
Skin tag	000/005	0.342	001/004	0.7874	002/003	0.7128
Tinea_Corporis	003/003	0.4449	003/003	0.3203	002/004	0.919
Vitiligo	001/002	0.6455	001/002	0.7324	000/003	0.7794
Wet gangrene	001/001	0.9153	000/002	1	000/002	0.919
Xanthelasma	001/005	0.8485	001/005	1	001/005	1
Lipodystrophy	002/001	0.3929	001/002	0.7324	000/003	0.7794

Conclusion

Regarding association of DM with other microangiopathic complications our study did not found any association of any kind of skin manifestations with DM. On the other hand, the study carried out by Mahajan *et al.* [15] found higher percentage of retinopathy (58.3%) and neuropathy (25%) among the patient with vasculopathic complication of DM. Another study carried out by Sawhney *et al.* [16] found though not statistically significant, dermopathy was more commonly associated with retinopathy (33.3% compared to only 13.7% who did not have dermopathy).

Goyal *et al.* [17] reported xerosis is predominant findings in hundred diabetic patients in Indian background. Ragunatha *et al.* found signs of insulin resistance, acrochordon (26.2%), and acanthosis nigricans (5%) as the most common presentation in 500 Indian diabetic cohorts [18]. But association of microangiopathic complications with skin lesions is not documented in any large-scale studies. Our study failed to reveal any association in this regard. More large-scale study involving more number of study populations may reveal this association in future.

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