IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 20, Issue 6 Ser.10 (June. 2021), PP 38-45
www.iosrjournals.org

A Comparative Study of Cutaneous Manifestations in Diabetes Mellitus Type 2 and Non Diabetic Patients: A Hospital Based Observational Study

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Abstract:

Background*: Diabetes mellitus is a group of metabolic disease with adverse effects on various systems including skin. Cutaneous manifestations among diabetes may correlate with diabetic control, duration and other complications. This study was undertaken to educate and raise awareness in patients to prevent long term complications by early diagnosis.*

Aims: *To study and compare cutaneous manifestations in patient with type 2 diabetes mellitus and Non-diabetic patients presenting to the outpatient and inpatient department of Mahatma Gandhi Medical College & Hospital, Jaipur.*

Methods: *The study was conducted at Mahatma Gandhi Medical College & Hospital, Jaipur (Rajasthan) India, over a period from January 2018 to April 2019. Six hundred patients were taken based on inclusion and exclusion criterias.*

Results: *Out of 600 patients studies, 300 were diabetes mellitus type 2 patient (cases) and 300 were Non-diabeties mellitus patients (control). Among the 300 diabetics studied, 223 (74.3%) were males and 77 (25.7%) were females with a Male:Female ratio 2.89:1. The result is not significant at P < 0.05. Maximum number of patients belonged to age group more than 60 years in both groups 27.7% in Diabetic group, 25.7% in Non-diabetic group. The result is not significant at P < 0.05.*

Conclusion: *Cutaneous manifestations of diabetes mellitus generally appear subsequent to the development of the disease, but they may be the first presenting signs and in some cases they may precede the primary disease manifestation by many years.*

Key Word*: Diabetes mellitus, Cutaneous markers, Dermatoses.*

Date of Submission: 06-06-2021 Date of Acceptance: 20-06-2021

I. Introduction

Diabetes mellitus is a group of metabolic disease associated with an impaired metabolism of carbohydrates, proteins and fat due to an absolute or relative deficiency of insulin secretion and / or insulin resistance and increased glucose production with chronic hyperglycemia.[1] It is most common endocrine disorder and have multisystem complications involving blood vessels, skin, eye, kidney and nervous system during the disease process. Association between cutaneous manifestations and diabetes mellitus ranges between 11.4% to 66%.[2] The International diabetic federation (IDF) predicts that total number of diabetic people in India will reach upto 101.2 million by year 2030.[3]

Classification of cutaneous manifestations in diabetes proposed by Sreedevi C [5]–

1. Strongly associated but not specific for diabetes (disease markers) - Diabetic bullae, Necrobiosis lipoidica diabeticorum, Granuloma annulare, Scleroderma like syndrome, Diabetic dermopathy and Pruritus
2. Due to diabetic complications - Diabetic foot, Cutaneous infections, Xanthomatosis, Xanthelasma, Phycomycetes and Malignant otitis media.
3. Due to neurovascular complications – Microangiopathy, Macroangiopathy, Diabetic neuropathy
4. Due to diabetes treatment - Oral hypoglycaemic drugs, Insulin
5. Endocrine syndromes with diabetes mellitus - Migratory necrolytic erythema
6. Commonly associated with diabetes mellitus – Psoriasis, Lichen planus, Vitiligo, Perforating dermatoses, Eruptive xanthomas, Bullous pemphigoid, Dermatitis herpetiformis, Kaposi sarcoma.

Hence, whenever a patient presents with multiple cutaneous manifestations, we must investigate for their diabetic status. We conducted this study to find out the prevalence of cutaneous manifestations in diabetes mellitus type 2 with non-diabetic patient and to educate and raise awareness in patients to prevent long term complications by early diagnosis.

II. Material And Methods

Hospital based observational study was conducted at **Department of Dermatology, Venerology and Leprosy**, **Department of Endocrinology** and **Department of General Medicine**, Mahatma Gandhi Medical College and Hospital, India over a period from January 2018 to April 2019. Total six hundred patients were taken, 300 each of diabetes mellitus type 2 patient (cases) and non-diabeties mellitus patients (control) based on inclusion and exclusion criterias. **Institute Ethics Committee approval was obtained.** Written and informed consent was obtained from all participants before enrolment into the study.

Inclusion Criteria:
All old and new confirmed patient of diabetes mellitus type 2, presenting to the outpatient and inpatient department of Mahatma Gandhi Medical College & Hospital.

Exclusion Criteria:
(a) Patients not consenting to the study
(b) Type 1 diabetes mellitus
(c) Gestational diabetes
(d) Immuno-compromised patients
(e) Any Malignancy

Detailed history, physical examination, systemic examination and cutaneous examination were done in all patients. Data was entered in Microsoft Office Excel worksheet. Appropriate statistical test chi-square was used to find out significant association and p value < 0.05 considered statistically significant.
The various investigations were done like Fasting blood sugar (FBS), Post-prandial blood sugar (PPBS), Glycated haemoglobin (HbA1c), Urine Routine examination/ microscopic examination and any required cutaneous investigation like Skin Biopsies, woods lamp and KOH were done when indicated.

III. Observation and Result

Among the 300 diabetics studied, 223 (74.3%) were males and 77 (25.7%) were females with a male : female ratio 2.89:1. The result is not significant at P< 0.05. Maximum number of patients belonged to age group more than 60 years in both groups 27.7% in diabetic group, 25.7% in non diabetic group. The result is not significant at P < 0.05. Among area wise distribution of both urban and rural diabetic patient did not show any statistically significant difference, result not significant at P<0.05. Maximum diabetic 233 (77.7%) patients had duration of diabetes between 1 to 10 years, among this newly diagnosed cases were 31 (10.3%) based on cutaneous manifestations. Among 300 diabetic group 139 (46.3%) had a positive family history of diabetes mellitus while out of 300 non diabetics 47 (15.7%) had a positive family history showing the result is highly significant at P <0.05.

Among the associated comorbidities, maximum were seen in diabetic group 42.75% then non diabetic group 24.3%, showed highly significant result P < 0.05. Among these pattern hypertension was most common disease seen in 67 (52.3%) diabetics followed by obesity 31(24.2%) and dyslipidemia in 13 (10.1 %) patients. Other systemic disorders found in our study were hypothyroidism in 10 (7.8 %) bronchial asthma in 5 (3.9%) and tuberculosis in 6 (1.25%) patients. The result is highly significant at P < 0.05. Out of 300 diabetic patients, 84 (28%) patients had fasting blood sugar (FBS) (mg/dl) < 126 considered as controlled diabetes while 216 (72%) patients had FBS >126 which was considered uncontrolled diabetes, similarly HbA1C <7 seen among 58 (19.4%) patient considered as controlled group and HbA1C >7 seen in 242 (80.7%) which was considered as uncontrolled group. Common dermatoses observed in diabetics and non diabetics patients are shown in Table 1 and Figure 1-3. Comparison of the incidence of the common cutaneous manifestations between cases and controls are shown in Table 2 and Figure 4.

Table 1: COMMON DERMATOSES OBSERVED IN THE DIABETICS AND NON DIABETICS PATIENTS

Cutaneous manifestations	Diabetic patients		Non diabetic patients	
Cutaneous infection & infestation-	No. of Case (n=300)	Percentage (%)	No. of Control (n=300)	Percentage (%)
Fungal infections				

Cutaneous manifestations	**Diabetic patients**		**Non diabetic patients**	
Cutaneous infection & infestation-	**No. of Case (n=300)**	**Percentage (%)**	**No. of Control (n=300)**	**Percentage (%)**
Dermatophytic infections	56	18.7	67	22.3
Candidal infection	47	15.7	21	7
Pityriasisversicolor	10	3.3	9	3
Bacterial infections				
Folliculities	14	4.7	9	3
Cellulities	10	3.3	5	1.7
Hansen's disease	4	1.3	5	1.7
Furuncle	1	0.3	0	0
Carbuncle	1	0.3	0	0
Erysipelas	1	0.3	0	0
Viral infections				
Herpes zoster	5	1.7	4	1.3
Varicella	1	0.3	2	0.7
Verruca vulgaris	1	0.3	1	0.3
Total number of infection	**151**	**50.3**	**121**	**41**
Parasitic infestations				
Scabies	5	1.7	4	1.3
Cutaneous changes associated with neurovascular changes				
Diabetic foot	13	4.3	0	0
Diabetic dermopathy	10	3.3	0	0
Pigmented purpuricdermatosis (PPD)	3	1	0	0
Cutaneous changes that may be associated with Diabetes Mellitus				
Acrochordons	93	31	56	18.7
Xerosis	65	21.7	25	8.3
Acanthosisnigricans	46	15.3	27	9
Pruritus	28	9.3	19	6.3
Kyrle's disease	13	4.3	2	0.7
Vitiligo	6	2	5	1.7
Psoriasis	4	1.3	5	1.7
Diabetic bullae	4	1.3	0	0
Xanthelasma	1	0.3	2	0.7
Miscellaneous				
Cherry angioma	34	11.3	26	8.7
Eczemas	31	10.3	42	14
Androgenetic Alopecia (AGA)	9	3	8	2.7
Pyoderma	7	2.3	4	1.3
Polymorphic Light Eruption (PMLE)	7	2.3	9	3
Urticaria	6	2	5	1.7
Granuloma annulare	6	2	1	0.3
Burning sensation over foot	5	1.7	1	0.3
Lichen planus	4	1.3	2	0.7
Seborrheiccapities	3	1	1	0.3
Bullous pemphigoid	3	1	1	0.3
Senile purpura	3	1	2	0.7
Alopecia areata	2	0.7	3	1
Mucormycosis	1	0.3	0	0
Perniosis	1	0.3	4	1.3
Discoid lupus erythematosis	1	0.3	0	0
Xanthomas	1	0.3	0	0
Erythema nodosum	1	0.3	1	0.3

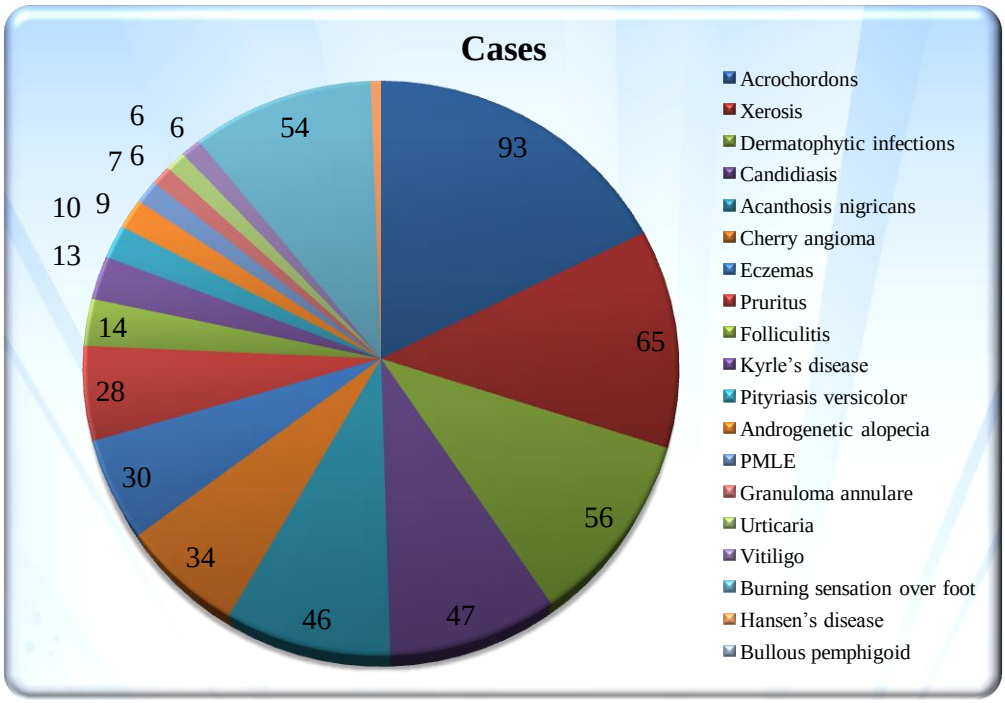
Figure 1 - Acrochordons with AcanthosisNigricans

Figure 2- Candidal Balanoposthitis

Figure 3 – Erysipelas

Table 2: COMPARISION OF FREQUENCIES OF THE COMMON CUTANEOUS MANIFESTATIONS BETWEEN CASES AND CONTROLS

Cutaneous manifestations	Frequency in cases (%)	Percentage (%)	Frequency in controls (%)	Percentage (%)	P - value
Acrochordons	93	(31%)	56	(18.7%)	**0.0004**
Xerosis	65	(21.7%)	25	(8.3%)	**0.0001**
Dermatophytic infections	56	(18.7%)	67	(22.3%)	0.265
Candidiasis	47	(15.7%)	21	(7%)	**0.00813**
Acanthosisnigricans	46	(15.3%)	27	(9%)	0.176
Cherry angioma	34	(11.3%)	26	(8.7%)	0.2763
Eczemas	30	(10%)	42	(14%)	0.131
Pruritus	28	(9.3%)	19	(6.3%)	0.171
Folliculitis	14	(4.7%)	9	(3%)	0.287
Kyrle's disease	13	(4.3%)	2	(0.7%)	**0.004**
Pityriasisversicolor	10	(3.3%)	9	(3%)	0.815
Androgenetic alopecia	9	(3%)	8	(2.7%)	0.805
PMLE	7	(2.3%)	9	(3%)	0.612
Granuloma annulare	6	(2%)	1	(0.3%)	0.573
Urticaria	6	(2%)	5	(1.7%)	0.760
Vitiligo	6	(2%)	5	(1.7%)	0.760
Burning sensation over foot	5	(1.7%)	1	(0.3%)	0.1007
Hansen's disease	4	(1.3%)	5	(1.7%)	0.736
Bullous pemphigoid	3	(1%)	1	(0.3%)	0.3157



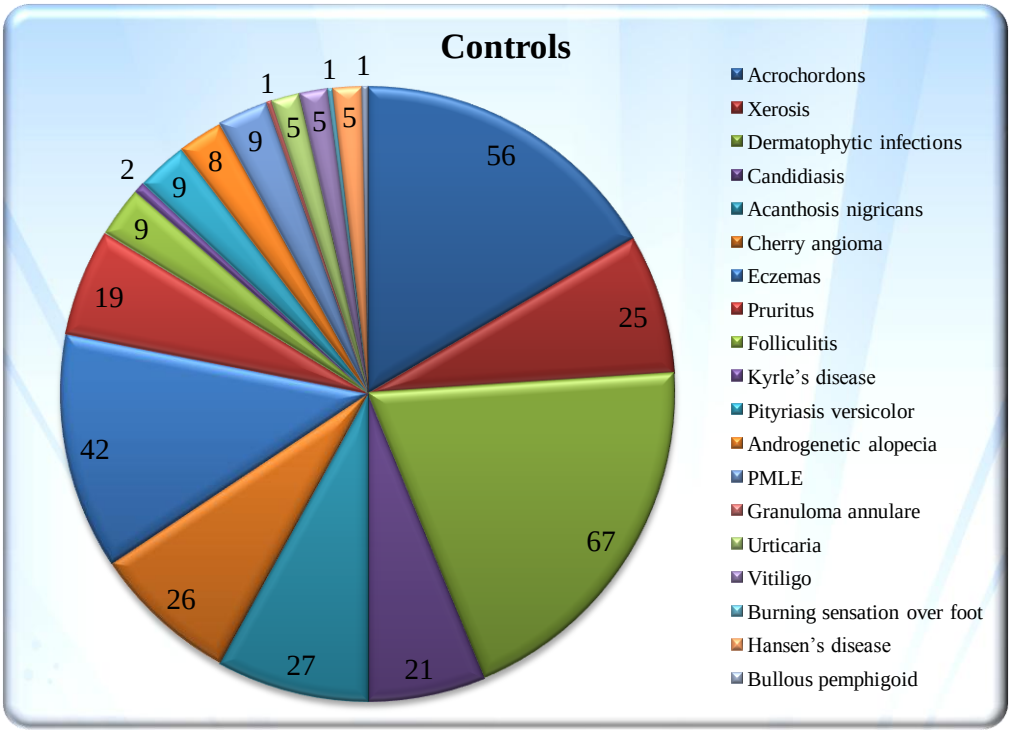


Figure 4 : COMPARISION OF FREQUENCIES OF THE COMMON CUTANEOUS MANIFESTATIONS BETWEEN CASES AND CONTROL

IV. Discussion

Skin manifestations in diabetes patients can occur prior to, with or after development of primary disease, but usually these findings occurs several years after the development of primary disease.[6]

In our study out of 300 diabetic patient most of the patient were in 5th and 6th decade. Maximum number of cases encountered were in the age group of more than 60 years (27.7 %) followed by the age group of 51 to 60 years (27.3 %). In a study by *Banavasi et al* [6] in 2017 similar finding of maximum patients in the age group of fifth and sixth decades of life with mean age 57.4+ 11.6 years were present.[6]

In a study done by *Kaur et al* [7] male to female ratio was 2.12:1 and study by *Nigam et al* [8] male to female ratio was 1.6:1. In our study out of 300 patient, 223 were males and 77 were female with male:female ratio being 2.89:1. In our study, out of 300 patients 156 (52 %) were of urban background and 144 (48 %) patients were of rural background.

In study by *Kaur et al* [7] among total 200 diabetes patients 26 were newly diagnosed, 62 patients (31%) had more than 10 years duration and maximum patients 112 (56%) had duration of 1-10 years. Similar finding were observed in our study where among 300 diabetes, 31 patients (10.3%) were newly diagnosed and 233 patient (77.7%) had duration of upto 10 years and 36 patients (12%) had duration more than 10 years. In study by *Ahmed et al*,[9] 63% patients had duration of 1-10 years whereas 37% had duration of more than 10 years, which is similar to our study.

In our study family history of diabetes was seen in 94 (31.3%) diabetic patients whereas it was seen in only 45(15%) patients in control group which was statistically significant (p value). Similar finding was seen in study by *Banavasi et al* [6] where 24.75% diabetic patient had a positive family history of diabetes. Presence of family history of type 2 diabetes mellitus is a well established risk factor for developing the disease.[10] Risk of developing type 2 diabetes mellitus increases approximately two to four fold when one or both parents are affected.[11,12]

In study done by *Balasubramaniyan et al*,[13] associated co-morbidities were seen in 176 (58.7 %) of diabetic patients and 20 (20 %) that of non-diabetic group. Among which hypertension was most common comorbidity seen in 130 (43%) cases followed by dyslipidemia seen in 83 (27.7%) cases. Whereas in our study, hypertension was seen in 67 (69.1%) followed by obesity seen in 31(24.2%) patients and dyslipidemia were seen in 13 (10.1%) diabetic patients as compared to 20 (27.4%) non- diabetic patient.

In our study uncontrolled diabetes was seen among 242 (80.7 %) patients whereas 58 (19.3 %) were controlled diabetics. In study by *Ahmad et al* [15] unsatisfactory glycemic control was seen in 137 (68%) patient which is similar to our study. In our study most common dermatological finding in diabetes group was infection seen in 151 (50.3 %), among which fungal infection was more common, dermatophytosis was seen in 56 (18.7 %) patients and candidiasis in 47 (15.7 %) patients. Next to fungal infection, bacterial infection was most

common whereas in control group fungal infection was seen in 32.3 % and bacterial infection in 6.4%. Infection was more common in patients with unsatisfactory glycemic index (50.3 %). Similar finding was seen in study by *Banavasi et al*[6] where fungal infection was seen in 106 (26.5%) patients and bacterial infection was seen in 27(6.75%) patients.

In our diabetic group, acrochordons was the second most common dermatoses in 93 (31%) patients followed by xerosis in 65 (21.7%) patients and acanthosis nigricans in 46 (15.3%) patients. Whereas in control group acrochordon was seen in 56 (18.7%) followed by acanthosis nigricans in 27 (9%) and xerosis in 25 (8.3%) patients. This difference signifies the correlation of diabetes with these skin findings. In a study done by *Ahmad et al*,[9] acanthosis nigrican was second most common dermatosis seen in 40 (20%) type 2 diabetic patient followed by acrochordon in 21(10%) patients, as contrary to our study. Similarly in a study done by *Mahajan et al*,[18] acrochordons were seen in 32% patients. Acrochordons may serve as a marker for diabetes mellitus as concluded by *Timshina et al.* [19]

In a study by *Kaur et al,* [7] they found xerosis as the third most common manifestation seen in 13.5%, which is slightly more than our study (8.3%), but it was also third most common manifestation in our study.

Following this, in a study done by *Kaur et al* [7] they found incidence of cherry angioma in 56(44.8%) cases in diabetic group and 50 (40%) cases in non-diabetic group, whereas it was less in our study where cherry angioma were seen in 34 (11.3%) diabetic cases and 26 (8.7 %) non-diabetic patients. This shows no definitive relationship between diabetic and non-diabetic patients in view of cherry angiomas. But this can be an indicator for development of diabetes in future.

In our study, eczema was seen in 30 (10 %) patients whereas in control group it was seen in 42 (14 %) patients.

In a study done by *Banavasi et al* [6] 3% patient had diabetic foot whereas in our study 13(4.3%) patient had diabetic foot, which is almost similar to that of *Ahmad et al* [9] where 16% patient had diabetic foot, which was much more.

In present study diabetic dermopathy was seen in 10 (3.3%) patients which was much less than the study done by *Mahajan et al* [18] where 30% patients and in *Balvinder et al* [7] 14.5% patients had this finding. But in study done by *Banavasi et al* [6] 0.5% cases showed diabetic dermopathy which was much less than our study.

In a study done by *Ahmad et al* [9] pruritus was seen in 8% case which was similar to our study where 28(9%) diabetes patient had pruritus. Whereas in study by *Mutairi et al* [21] 47% diabetic patient had pruritus, whereas in control group 19 (6.3%) patients had pruritus.

Kyrle's disease (acquired perforating dermatosis) in our study was present in 13 (4.3%) patients, whereas in control it was seen 2 (0.7%) patients which suggested a strong relationship between kyrle's disease and uncontrolled diabetic. Androgenetic alopecia (AGA) in our study was present in 9(3%) patients whereas it was present in 8 (2.7%) non-diabetic patient. Polymorphic light eruption (PMLE) was present in 7 (2.3%) diabetic patients whereas in non-diabetic it was seen in 9 (3%) patients. Granuloma annulare and urticaria was present in 6 (2%) diabetic patients each.

Dermatological manifestation having a frequency less than 5% were : pigmented purpuric dermatitis 0.3%, psoriasis 1.3%, vitiligo 2%, xanthelesma 0.3%, diabetic bullae 1.3%, bullous pemphigoid 1%, burning sensation over feet 1.7%, discoid lupus erythematous 0.3%, granuloma annulare 2%, lichen planus 1.3%, seborrheic capities 1%, PMLE 2.3%, alopecia areata 0.7% xanthomas 0.3% and mucormycosis 0.3%.

Vitiligo and lichen planus were not associated with diabetes mellitus in our study. In study by *Timshina et al* [19] which included patient with both type 1 and type 2 diabetes mellitus, vitiligo was associated with diabetes, whereas lichen planus was not associated.

Our study also helped in diagnosis of 31(10.3%) new cases of diabetes, patients were investigated on strong suspicion due to persistent or recurrent skin manifestations such as recurrent balanoposthitis, diabetic bullae, diabetic dermopathy, giant granuloma annulare, patients of persistent and severe fungal & bacterial infections, necrobiosis lipoidica, diabetic dermopathy, yellow nails and acanthosis nigricans, whereas eruptive xanthomas reflect the status of glucose and lipid metabolism.

V. Conclusion

Certain Skin manifestations can be an initial finding and presenting sign which may help in early diagnosis of diabetes mellitus. Hence, whenever a patient presents with such skin conditions, one must investigate for the diabetes status as the study shows that frequency of cutaneous infections and incidence of certain dermatoses were higher among the diabetics than among non diabetics. Therefore, this study facilitates early diagnosis of diabetes among the patients and may be helpful in improving their quality of life.

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Manmohan Bagri, et. al. "A Comparative Study of Cutaneous Manifestations in Diabetes Mellitus Type 2 and Non Diabetic Patients: A Hospital Based Observational Study."*IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 20(06), 2021, pp. 38-45.