

PATTERN OF CUTANEOUS (FUNGAL AND VIRAL) MANIFESTATIONS IN DIABETES MELLITUS AND ITS CORRELATION WITH GLYCOSYLATED HEMOGLOBIN LEVELS

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ABSTRACT

Background: Diabetes mellitus (DM) is the most common endocrinal disorder and is associated with a plethora of skin manifestations. The objective of our study was to determine the cutaneous fungal and viral manifestations of diabetes mellitus and their correlation with glycosylated hemoglobin (HbA1c) levels. **Material and Methods:** A total of 64 diabetic patients with cutaneous manifestations were studied. A detailed history and relevant investigations were done. The results were tabulated in tables and graphs. A chi-square test was used to correlate the skin manifestations with HbA1c levels. **Results and Discussion:** Among the 64 patients, majority of the patients were males and most of them belonged to the age group of 41-50 years. In the cutaneous spectrum studied, fungal infections were common in cutaneous infections. Most of the patients with skin manifestations had fair to poor control of diabetes mellitus (HbA1c > 7). There was a statistical significance in the HbA1c values obtained from those who had cutaneous fungal infections. **Conclusion:** The skin manifestations in diabetes mellitus are vast and extremely variable. They generally appear after the primary disease has developed but may signal or appear co-incidentally with diabetes. Our study highlights the importance of knowing the various skin manifestations in diabetes mellitus, which helps in early diagnosis and treatment of the condition, thereby preventing complications.

KEYWORDS: Diabetes mellitus, Glycosylated hemoglobin, Cutaneous Manifestations.

INTRODUCTION

Diabetes mellitus is the most common endocrine disorder. It affects individuals of all ages and in all socioeconomic segments of the population. Globally, the number of people with diabetes mellitus has quadrupled in the past three decades and has emerged as a major public health problem in our country, and our country has a distinction of having the largest number of diabetics in the world to be around 72.9 million in India and the number is expected to rise to 101.2 million by the year 2030.^[1]

The epidemic of diabetes mellitus and its complications poses a major global health threat owing to the present scenario of sedentary lifestyles in the general population. Abnormalities of insulin and elevated blood glucose levels lead to metabolic, vascular, neurological and immunological abnormalities including the skin. Skin is affected by both the acute metabolic derangements and the chronic degenerative

complications of diabetes. Though skin manifestations can be the first presenting sign of diabetes, they are more frequently seen in known diabetic cases during the course of the disease.

Individuals with type 2 diabetes are more likely than those with type 1 diabetes to develop cutaneous manifestations. *Perez MI et. al.* reported that at least 30% of persons with diabetes have some type of cutaneous involvement during the course of their chronic disease and they broadly classified cutaneous findings of diabetes mellitus into four categories.^[2]

- 1) Skin diseases with strong to weak association with diabetes mellitus: Necrobiosis lipiodica, Diabetic dermopathy, Diabetic bullae, yellow skin, Eruptive xanthomas, Perforating disorders, Acanthosis nigricans, Oral leucoplakia and Lichen planus).
- 2) Cutaneous infections: Bacterial, Fungal and viral.
- 3) Cutaneous manifestations of diabetic complications: Microangiopathy, Macroangiopathy and Neuropathy.

- 4) Skin reactions to diabetic treatment: Sulphonylureas or Insulin.

In this study we are targeting the cutaneous fungal and viral infections in Type 2 diabetes patients.

1. Fungal infections

- a) **Candidial infection:** Mucocutaneous candidal infections occur more frequently among patients with diabetes mellitus, especially those with poorly controlled disease.^[3] Candidial infection (moniliasis) can be an early sign of undiagnosed diabetes. Paronychia, onychomycosis, pruritus ani and oral candidiasis are also common.
- b) **Dermatophytosis:** Association of dermatophyte infection with diabetes is controversial but recent data shows a statistically significant relationship.^[4] According to *Jolly et. al.*, trichophyton rubrum infections are more common in diabetics and *Greenwood et. al.* reported that the incidence of dermatophytosis is about 40%. The other common superficial infections are caused by Trichophyton mentogrophytes, and Epidermophyton floccosum. In diabetic patients, onychomycosis or tinea pedis should be monitored and treated, as it can be a part of entry for infection.^[5]
- c) **Pityriasis versicolor:** This is an asymptomatic superficial fungal infection of stratum corneum caused by pityrosporum orbiculare which changes from the round budding blastospore to pathogenic hyphal form under the influence of high skin glucose level.^[6]
- d) **Phycomycetes infection:** Hyperglycemia permits the usually non-pathogenic organisms to establish infection in traumatized skin. Diabetic patients having leg ulcers or non-healing surgical wounds may have complicating phycomycetes infection.

Rhinocerebral mucormycosis (RCM) is caused by zygomycetes (mucor and rhizopus species) often presents with headache, fever and lethargy in addition to nasal congestion and facial, ocular pain and swelling. Also associated with ophthalmoplegia, palate and nasocutaneous necrosis. About 75-80% of all cases occur in patients with diabetes mellitus, with diabetic ketoacidosis as the most important risk factor.^[7]

2. Viral infections

Herpes zoster is the most common viral infection in diabetics. Diabetics are more susceptible to develop herpes zoster and it occurs at a younger age in diabetics, compared to the general population. This could be due to the depressed immune response in poorly controlled diabetes.^[8]

MATERIALS AND METHODS

Source of Data

The materials for the present study were drawn from patients who were diagnosed to have Type 2 diabetes mellitus, attending General medicine and Dermatology

outpatient department and those admitted in the Dermatology and General medicine of RIMS. Hospital, attached to Rajiv Gandhi Institute of Medical Sciences, Kadapa. The data was collected for a period of 6 months and a total of 64 patients were included in the study.

Inclusion criteria

All patients diagnosed (new and old) type 2 diabetes mellitus (fulfilling the Revised American Diabetic Association (ADA) criteria), presenting with cutaneous manifestations were included in the study.

Exclusion criteria

- Patients with gestational diabetes mellitus
- Type1 Diabetes mellitus
- Steroid induced diabetes mellitus
- Impaired glucose tolerance
- Diabetes mellitus following acute or chronic pancreatitis.

All the patients who were diagnosed to have diabetes mellitus according to the revised ADA criteria were subjected to the following:

- An informed consent was obtained.
- A detailed history with regards to the cutaneous complaints, duration, family history and treatment of diabetes mellitus were noted.
- Complete cutaneous and systemic examinations were done under good light.

The following relevant investigations were done: -

- a) Blood investigations: Fasting blood sugar (FBS), random blood sugar (RBS), postprandial blood sugar (PPBS), glycosylated hemoglobin (HbA1C) as well as LFT, RFT and lipid profile.
- b) Investigations done in relevant cases to diagnose cutaneous manifestations associated with DM like Gram's staining, Potassium hydroxide (KOH) mount, Wood's lamp, Skin biopsy, Tzanck smear.

RESULTS

A total 70 patients as per eligibility criteria were enrolled in the study. Among them, 6 patients were dropped out because of loss of follow up. Majority of the patients belonged to age group of 41-50 years (37.5%), followed by 51-60 years (29.6%), above 60 years (23.4%) and 31-40 years (9.4%) respectively as shown in table no.1

Table 1: Age distribution of patients.

Age group	No. of cases	Percentage
31 - 40	6	9.4
41 - 50	24	37.5
51 - 60	19	29.6
Above 60	15	23.4
Total	64	100.0

In the present study, 21 (32.8%) patients had diabetes of duration between 1-5 years, followed by 6-10 years in 18 (28.1%), >10 years in 12 (18.7%), <1 year in 5 (7.8%),

and 8 (12.5%) patients were newly diagnosed as shown in table no. 2.

Table 2: Duration of diabetes mellitus.

Duration of diabetes mellitus	No. of cases	Percentage
< 1 yr	5	7.8
1 - 5 yrs	21	32.8
6 - 10 yrs	18	28.1
> 10 yrs	12	18.7
Newly Diagnosed	8	12.5
Total	64	100.0

The most commonly associated systemic condition was hypertension, seen in 7 (10.9) patients, followed by 6 (9.4%) patients with Dyslipidemias, ischemic heart disease 3 (4.7%), nephropathy 2 (3.12%), peripheral vascular disease 1 (1.56%) patients, retinopathy 1(1.56%) patient, neuropathy 1 (1.56%) as shown in table no.3.

Table 3: Various systemic associations with diabetes.

Various Systemic associations	No. of cases	Percentage
Hypertension (HTN)	7	10.9
Dyslipidemias	6	9.4
Ischaemic heart disease (IHD)	3	4.7
Peripheral vascular disease (PVD)	1	1.56
Neuropathy	1	1.56
Retinopathy	1	1.56
Nephropathy	2	3.12
Total	21/64	32.8/100

Spectrum of Fungal and Viral infections

Out of 64 patients, 54 (84.3%) accounted for fungal infections and 10 (15.7%) were viral infections as shown in figures 1 & 2 respectively. Candidal balanoposthitis was seen in 12 patients, followed by 10 patients of candidal intertrigo, 4 patients of tinea corporis, tinea

versicolor 6 patients, 2 patients each of onychomycosis, tinea cruris 8 patients, tinea pedis, Candidal vulvovaginitis, Tinea mannum, Mucor mycosis each accounting for 2 patients whereas in viral infections, herpes zoster accounted for 6 patients and herpes labialis / Genitalis was seen in 4 patients.

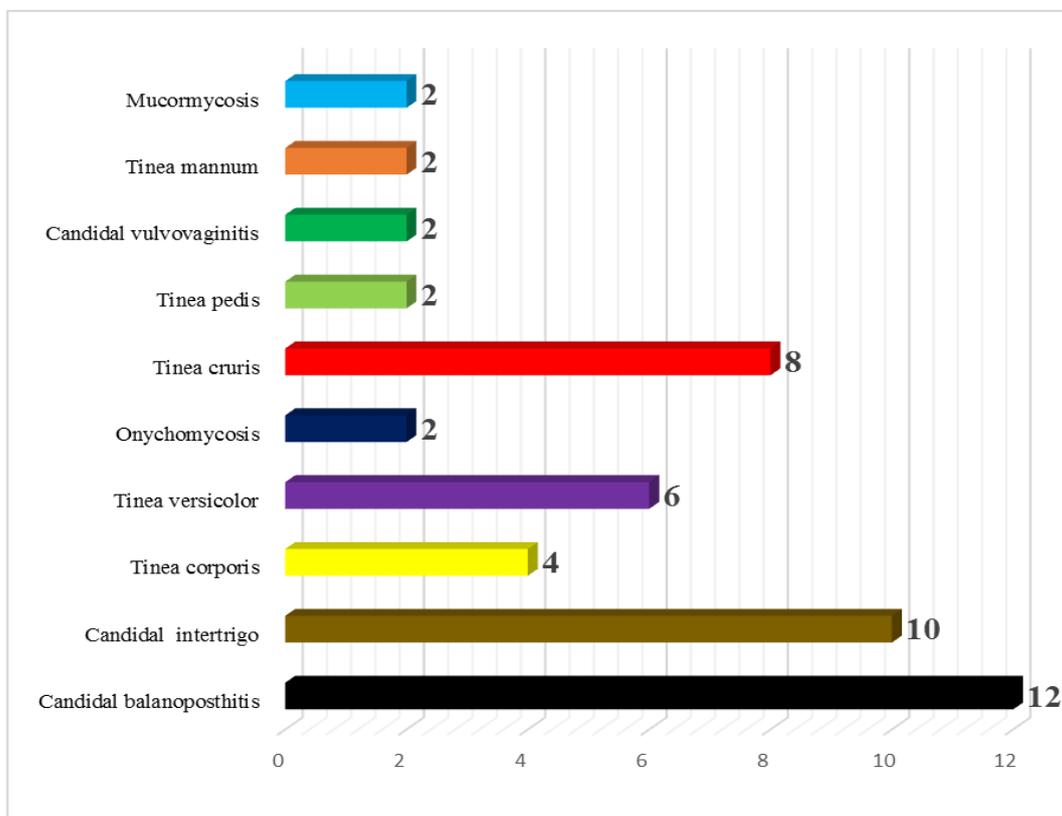


Figure 1: Spectrum of Fungal Infections.

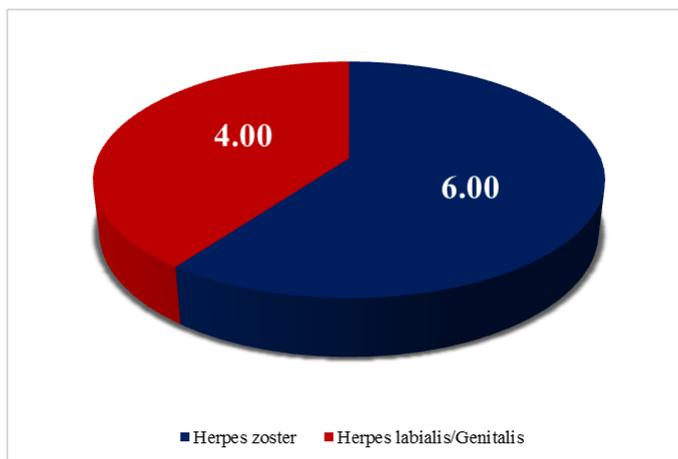


Figure 2: Spectrum of Viral Infections.



Figure 3: Herpes Zoster.



Figure 4: Herpes Zoster.

Glycosylated hemoglobin levels

Glycosylated hemoglobin was done for all the patients of which 29 (45.3%) patients had fair control (7.01 – 8.0%), 21 (32.8%) patients had good control, 11 (17.2%) patients had poor control (>8.0%) and 3 (4.7%) patients had normal values (<6%).

Table 4: Glycosylated hemoglobin levels.

Glycosylated hemoglobin levels	No. of cases	Percentage
< 6 % (Normal)	3	4.7
6.01 - 7 % (Good control)	21	32.8
7.01 - 8 % (Fair control)	29	45.3
> 8 % (Poor control)	11	17.2
Total	64	100.0

Blood sugar levels

The mean random blood sugar was 214.92 ± 75.08. The mean fasting and postprandial blood sugar was 145.44 ± 44.65 and 217.34 ± 55.05 respectively.

Table 5: Blood sugar levels.

Blood sugar levels	Minimum	Maximum	Mean ± S.D
RBS (mg/dl)	70	622	214.92 ± 75.08
FBS (mg/dl)	81	360	145.44 ± 44.65
PPBS (mg/dl)	140	464	217.34 ± 55.05

Correlation of cutaneous manifestations with glycosylated hemoglobin

Glycosylated hemoglobin values were obtained from all patients. A chi-square test done on the data showed a statistical significance (p-value = 0.038) between fungal infections and glycosylated hemoglobin levels. Majority of the patients with cutaneous fungal infections had higher glycosylated hemoglobin values. Majority of the cutaneous manifestations (45.3%) were seen in patients with fair to poor control compared to (4.7% + 32.8%) in patients with normal to good control.

Table 6: Correlation of cutaneous manifestations with glycosylated hemoglobin.

Spectrum of cutaneous manifestations	Normal		Good Control		Fair Control		Poor Control		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%
Fungal Infections	3	4.7	18	28.12	24	37.5	9	14.06	54	84.3%
Viral Infections	0	0.00	3	4.7	5	7.8	2	3.12	10	15.7%
Total	3	7.8	21	32.8	29	45.3	11	17.2	64	100.00

DISCUSSION

In the present study of 64 patients of diabetes mellitus, majority of the patients (37.5%) belonged to the age group of 41-50 years, 51-60 years accounted for 29.6% of patients, and above 60 years accounted for 23.4% of patients. **Mahajan et al**^[9] also reported similar frequencies of 33% and 30% for age groups between 41-50 years and 51-60 years respectively. Similar frequencies were also reported by **Al-Mutairi et al**,^[10] **Nigam et al**^[11] and **Timshina et al**.^[12] The increase in frequency of cutaneous involvement with age may be attributed to the long duration of diabetes in this group of patients, as chronicity of DM plays a big role in the cutaneous manifestations.^[13] Mean age of onset of type 2 DM in the present study was 47.56 ± 7.5 years of age. **Shahzad et al**^[14] reported a mean age of onset of 50.82 ± 11.28 years of age for type 2DM.

In the present study, most of the patients (28.1%) had diabetes with duration of 6-10 years, which was similar to the findings reported by **Timshina et al**.^[12] Diabetes mellitus of duration upto 10 years accounted for 84.5%, 60.9%, and 83.3% of the patients in the studies conducted by **Bhat et al**,^[15] **Ahmed et al**^[16] and **Timshina et al**.^[12] Thus, the results of the present study are in well accordance with the above-mentioned studies.

In the present study, out of 64 patients, 21 (32.8%) patients had associated systemic co-morbidities, most common being hypertension seen in 7 patients. Similarly, **Mahajan et al**^[9] (53.1%), **Bhat et al**^[15] (46.4%) and **Al-Mutairi et al**^[10] (44%) also reported hypertension to be the most common systemic co-morbidity associated with diabetes mellitus. Hypertension has been known to hasten the process of microangiopathy in diabetics.^[7,2]

Fungal infections were seen in 54 out of 64 (84.3%) patients, which formed the majority. Similar findings were also reported by **Bhat et al**,^[15] **Mahajan et al**,^[9] **Al-Mutairi et al**^[10] and **Shahzad et al**.^[14] In the present study, candidal balanoposthitis was the most common fungal infection seen in 12 (18.75%) patients and candidal infections comprised of 48% of all fungal infections, which is in accordance with the observations of **Goyal et al**^[17] (56.25%) and **Bhat et al**.^[15]

In the present study, 10 patients had viral infections, 6 (9.3%) of them had herpes zoster and 4 (6.25%) patient had herpes labialis/Genitalis. **Mahajan et al**^[9] reported only 2 cases (2%) of herpes zoster in their study. **Al-Mutairi et al**^[10] and **Bhat et al**^[15] reported 3 cases each of herpes simplex.

In the present study, 29 (45.3%) of patients had fair (moderate) control, 21 patients (32.8%) had good control, 17.2% had poor control and 4.7% had normal values. Similar findings were reported by **Vahora et al**^[13] (55%) and **Nigam et al**^[11] (52%).

Timshina et al^[12] and **Ragunatha et al**^[18] found majority of the patients having good control of diabetes. Uncontrolled diabetes mellitus predisposes skin for various infections and also increases the risk of microangiopathy and related complications.^[15]

Statistical significance (p-value = 0.038) was found between fungal infections and HbA1c levels; with majority of the patients (62.5%) showing fair to poor control of diabetes. **Bhat et al**^[15] also reported most of the patients with cutaneous infections having poor control of diabetes. **Farshchian et al**^[19] did not report any significant relationship between glycemic control and prevalence of cutaneous infections.

In the present study, 37.5% of the patients with cutaneous manifestations had normal to good control of diabetes, whereas fair to poor control accounted for 62.5% of the cases. Hence, majority of the cases with cutaneous manifestations had fair to poor control. **Bhat et al**^[15] and **Nigam et al**^[11] also reported higher incidence of cutaneous manifestations in patients with uncontrolled diabetes with incidence of 55.6% and 52% respectively; which are in concordance with the results of the present study.

The present study is in concordance with the above-mentioned studies. It is well known that diabetic patients are susceptible to infections,^[20] but surprisingly, viral infections in diabetics have not been reported frequently in previous studies as compared to bacterial and fungal infections. The exact reason for this is not known.

CONCLUSION

A good glycemic control definitely reduces the incidence and severity of cutaneous disorders with or without known pathogenesis. However, several nonspecific cutaneous disorders that occur in diabetic patients can increase the likelihood of exposure to infectious organisms and contact allergens, resulting in chronic and recurrent infections and eczemas, respectively. These further worsen the diabetes control of the patients. Thus, physician plays an important role in reducing morbidity, improvement of quality of life and management strategy of diabetic patients. It is necessary to have a physician in the diabetic clinic for early detection of potentially grave or predisposing conditions and to provide a comprehensive diabetic care to the patients.

The cutaneous manifestations in diabetes mellitus are numerous and varied. Not only can dermatologic symptoms help identify and treat skin disorders associated with diabetic mellitus, they also can be important for the initial diagnosis of the underlying disease, even though no skin diseases are specific to diabetic mellitus.

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