

Original research article**A Descriptive Study of Various Mucocutaneous Manifestations in Diabetes Mellitus****Dr. Smita Prasad¹, Dr. Pankaj Tiwari², Dr. Anupama Singh³**¹Assistant Prof. Department of Dermatology, PMCH Patna²Assistant Prof. Department of Dermatology, PMCH Patna³Assistant Prof. Department of Dermatology, PMCH Patna**Corresponding Author: Dr. Smita Prasad****Abstract**

Background: Diabetes mellitus is characterized by chronic hyperglycemia with disturbances of carbohydrate, fat, and protein metabolism resulting from defects in insulin secretion, insulin action, or both.⁴ Insulin is essentially the only hormone that can lower blood glucose. This study has undertaken with the objectives of knowing the spectrum of mucocutaneous manifestations in diabetes mellitus.

Methods : Out of 100 patients with dermatological manifestation were included in the study. Relevant investigation for the diagnosis of diabetes and dermatological disorders were done.

Conclusion: Thus, dermatologists can play an important role in reducing dermatologic morbidity, improvement of quality of life, and management strategy of diabetic patients.

Keywords: Diabetes; Mucocutaneous Manifestations.

Introduction

The skin is the largest and the most visible organ of the body. It is a well-known fact that the skin is referred to as window or mirror to the body. Diabetes mellitus (DM) is a worldwide problem and the most common endocrine disorder. Its prevalence is increasing in the present scenario of a sedentary life style 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. 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. Skin manifestations can be the first presenting sign of diabetes but more often appear in known diabetic patients during the course of the disease. As observed in 30–71% of diabetic patients. The mucocutaneous manifestations of DM are well known and considered common. This study is an attempt to analyze the pattern of mucocutaneous manifestations of diabetes in view of the increasing prevalence of diabetes in the present scenario lifestyle in the general population.

Objectives

To study the clinical pattern of mucocutaneous manifestations in patients of Diabetes Mellitus.
To study the relation of these mucocutaneous manifestations with demographic data like age, sex and duration of Diabetes.

Review of Literature

The word “diabetes” was 1st used by **Aretaeus of Cappadocia** in the 2nd century AD. It comes from the Greek, meaning syphon. Aretaeus gave a clinical description of the disease, noting the increased urine flow, thirst and weight loss, features that are instantly recognizable today.¹ The sweet, honey - like taste of urine in polyuric states, which attracted ants and other insects, was reported by Hindu physicians such as **Sushrut (Susruta)** during the 5th and 6th centuries AD.² These descriptions even mention two forms of diabetes, the more common occurring in older, overweight and indolent people, and the other in lean people who did not survive for long. This empirical subdivision predicted the modern classification into type 1 and type 2 diabetes. Banting and Best’s notes of the dog experiments refer to the administration of isletin”, later called insulin by them at the suggestion of Macleod. They were unaware that the Belgian Jean de Meyer had already coined the term „insuline“ in 1909. (All these names ultimately derive from the Latin for „island“). The first sulfonylurea carbutamide was introduced in 1955, followed by tolbutamide in 1957 and chlorpropamide in 1960. The biguanidephenformin became available in 1959 and metformin in 1960.³ Diabetes mellitus is characterized by chronic hyperglycemia with disturbances of carbohydrate, fat, and protein metabolism resulting from defects in insulin secretion, insulin action, or both.⁴ Insulin is essentially the only hormone that can lower blood glucose. Diabetes is common and is becoming more common. Age - adjusted prevalence is set to rise from 5.9% to 7.1% (246 – 380 million) worldwide in the 20 – 79 year age group, a 55% increase. The relative proportions of type 1 to type 2 vary from 15:85 for Western populations to 5:95 in developing countries.⁵ WHO classification of DM and allied categories of glucose intolerance adopted in 1980 and modified in 1985 is as follows: ⁶

Diabetes mellitus

Insulin-dependent diabetes mellitus, Non-insulin-dependent diabetes mellitus, Non-obese

Table 1: Difference between Type 1 and Type 2 Diabetes⁷

Type 1 Diabetes	Type 2 Diabetes
Sudden onset with severe symptoms of thirst and ketoacidosis (vomiting, hyperventilation, dehydration)	Usually insidious onset of tiredness, thirst, polyuria, nocturia
Recent, marked weight loss	Often no recent weight loss
Usually lean	Usually overweight or obese
Spontaneous ketosis	Frequent infections, e.g. urine, skin, chest
Life-threatening; needs urgent insulin replacement	Symptoms may be minimal and/ignored by patient
Absent C peptide	C peptide detectable
Markers of autoimmunity present (e.g.-islet cell antibodies)	No markers of autoimmunity. Often other features of metabolic syndrome, e.g hypertension

According to recent estimates, approximately 285 million people worldwide (6.6%) in the 20-

79 year age group will have diabetes in 2010 and by 2030, 438 million people (7.8%) of the adult population, is expected to have diabetes. The largest increases will take place in the regions dominated by developing economies⁸ About 80% of type 2 diabetic subjects are obese, and the risk of developing diabetes increases progressively as the body mass index [BMI, weight/height(m²)] increases. BMI > 35 kg/m² increases the risk of type 2 diabetes developing over a 10 - year period by 80 - fold, as compared to those with a BMI < 22 kg/m² . The pattern of obesity is also important in that central fat deposition has a much higher risk for development of diabetes compared to gluteofemoral deposition.⁹ In clinical practice, HbA1c provides an objective measure of long-term glycemic control in a single measurement. As a result of the links established between control and tissue complications by major trials in type 1 and type 2 diabetes, the HbA1c level can also be regarded as a risk factor for the development of microangiopathy.¹⁰ The American Diabetes Association recommends that the goal of diabetes therapy should be to achieve an HbA1c <7%, and that the treatment action should be taken when values are consistently >8% .¹¹ Dermatologic disorders associated with DM generally appear after the primary disease or they may signal or appear coincidentally with its onset, or even precede DM by many years. The mucocutaneous clinical signs are numerous and varied as 1/3rd of patients with diabetes are estimated to have cutaneous changes.¹² No disease of skin is absolutely peculiar to diabetes, yet there are diseases, the incidence of which is more in diabetics than in non-diabetics.¹³ Skin involvement of diabetes mellitus is very common and some form of cutaneous involvement has been found in 43-66% of Indian diabetics.^{14,15} Although, the overall prevalence is the same in IDDM and NIDDM patients, congenital or acquired total lipodystrophy with loss of subcutaneous and visceral fat, hepatomegaly with abdominal prominence, acanthosis nigricans, increased bone growth, hypertrichosis, abundant curly scalp hair and insulin resistant non-ketotic DM. glucose intolerance can be detected earlier.¹⁶ This sign is more evident in the toe nails and is often associated with purpura, pigmentation, erythema and impending gangrene.¹⁷ The yellowing of nails probably represents glycosylation end products. This finding has not been confirmed yet, but one study of fingernails has demonstrated that diabetics have high levels of fructose-lysine, another marker for NEG.¹⁸

Material and methods

The study consisted of 100 cases of Type 1 and Type 2 Diabetes Mellitus with mucocutaneous manifestations attending Dermatology OPD & IPD, at Patna medical college and Hospital Patna, Bihar. Study duration of Six months.

Inclusion criteria

All confirmed (old and new) cases of Diabetes Mellitus with mucocutaneous manifestations irrespective of age, sex, duration of illness and associated diseases, willing to participate in the study.

Exclusion criteria:

Patients not willing to participate in the study Patient who are in terminal illness.

A sample size of 100 was selected and this was calculated by using the formula $4pq/d^2$ where p=prevalence, q=100-p, d=absolute error. In the selected patients, a detailed history with particular reference to demographic details, family history of similar complaints and of DM, duration of DM treatment details, duration of various symptoms and evolution of lesions was taken. The patients were clinically examined in good light, for various mucocutaneous manifestations of DM such as skin lesions, nail changes, mucous membrane involvement. Routine haematological and urine investigations such as Hb%, TC, DC, ESR, RBS, urine routine and microscopy were done in all patients. Fasting blood sugar (FBS), random blood

sugar (RBS), Glycosylated (glycated) haemoglobin (HbA1c). The culture medium used was the Sabouraud's Dextrose Agar (SDA), with a pH of 5.6, supplemented with antibiotics like chloramphenicol and gentamycin to prevent bacterial overgrowth. Freshly collected specimens were inoculated onto two tubes of SDA, and were incubated. In candida species, the growth appears in 3 to 4 days as cream coloured, smooth and pasty colonies.

Results

Table 2: Sex distribution of patients

Sex	No. of cases	Percentage (%)
Male	50	50
Female	50	50
Total	100	100

Among 100 patients studied 50 (50%) were males and 50 (50%) were females. The male to female ratio was 1

Table 3: Age distribution of the patients.

Age (years)	No. of cases	Percentage (%)
20-40	11	11
41-60	46	46
61-80	33	33
>80	10	10
TOTAL	100	100

In the present study, peak prevalence was seen in the age group of 41 -60 years that is 46%. Among 100 patients studied, 33 patients were in the age group of 61-80 years (33%), 11 patient were in 20-40 years (11%), 10 patient were above 80 years.

Table 4: Family history of diabetes

Family history	No. of patients	Percentage (%)
With family history	32	32
Without family history	68	68
Total	100	100

Among 100 patients, 68 (68%) of them had a family history of diabetes mellitus., 32% patients gave a negative family history.

Table 5: Bacterial infection

Bacterial infection	NUMBER
Furunculosis	3
Folliculitis	1
Cellulitis	6
Abscess	1
Carbuncle	1

Among the 100 diabetic patients, 12 had bacterial infections of which the most commonly observed were cases of cellulitis 6 cases, followed by furuncle 3 cases, and 1 case each of folliculitis, abscess and carbuncle.

Table 6: Viral infections

Viral infection	No. of cases	percentage
Verruca vulgaris	1	20
Herpes zoster	4	80

5 patients with viral infections, 1 (20%) patients had verruca vulgaris and 4 patients (80%) were diagnosed to have herpes zoster.

Table 7: Dermatoses commonly associated with DM

Dermatoses	No. of cases
Generalized pruritus	7
Psoriasis	3
Vitiligo	1
Lichen planus	3
Macular amyloidosis	1

Among the various dermatoses studied in 100 patients of DM, the most commonly associated with diabetes are shown in the table above. Majority presented with generalized pruritus 7 patients (7%), followed by psoriasis and lichen planus 3 cases each, 1 case each (1%) of macular amyloidosis and vitiligo.

Table 8: Dermatoses associated with neuropathy

Dermatoses	No. of cases	Percentage
Diabetic foot	2	2

2 patients had diabetic foot

Table 9: Dermatoses Associated With Microangiopathy

Dermatoses	No. of cases
Diabetic dermopathy (DD)	1
Granuloma annulare (GA)	1
Diabetic bullae	1

Out of 100 patients studied, one of each patients had Diabetic dermopathy (DD), Granuloma annulare (GA) and diabetic bullae respectively.

Table 10: Random blood sugar levels

RBS(mg/dl)	No. of cases	Percentage (%)
70-140	22	22
140-200	49	49
>200	29	29
Total	100	100

Majority of the patients had random blood sugar levels in the range of 140-200mg/dl (49%), followed by 29% patients with levels >200mg/dl.

FURUNCLE**TINEA CRURIS****Discussion**

In this study, ratio of male diabetics and females diabetics is (50 vs 50%), but male diabetics were prone for mucocutaneous involvement by Sawhney et al¹⁹, Rao et al²⁰ and Al-Mutairi et al.²¹ Mahajan et al¹⁵, Bhat et al²² and Nigam et al¹⁴ reported that female diabetic patients had significantly higher incidence of mucocutaneous manifestations. In this study of 100 patients of DM with mucocutaneous manifestations, majority belonged to 41-60 years with 46%. The frequencies of patients with mucocutaneous manifestations in the age group of 20-40 years (11%), 61-80 years (33%), and 10 patients were above 80 years respectively. Similar frequencies were reported by various studies carried out by Mahajan et al¹⁵, Sawhney et al¹⁹ and Nigam et al¹⁴, which are well in accordance with the above frequencies. The relative increase in the incidence of mucocutaneous involvement with age in diabetic patients may be attributed merely to the decreased resistance of body as well as long duration of diabetes in these patients. Non-insulin dependent diabetes mellitus (type 2 DM) was most commonly observed (98%) as compared to Insulin dependent diabetes mellitus (type 1 DM) (2%). This reflects the general distribution pattern of type 1 and type 2 DM cases in world population. No difference in the prevalence of mucocutaneous disorders between type 1 and type 2 DM patients has been noted.^{21,22} Similar observations of type 2 diabetes being more common was observed in studies conducted by Mahajan et al¹⁵ (98%), Sawhney et al¹⁹ (80%), Bhat et al²² (97.7%), Nigam et al¹⁴ (82.1%) and Al-Mutairi et al²¹ (93%). Thus the present study values are well in accordance with the above mentioned studies. In this study, a positive family history of diabetes mellitus was obtained in 32 patients (32%), while 68 patients (68%) gave a negative

family history, Among the 100 patients, majority of the patients were housewives (49%), followed by Un employee (18%), private employee and agriculturalist (13%), govt. employee (4%), Retired govt. employee (3%). In the present study, majority were housewives probably because of the sedentary lifestyle and lack of exercise, so also in an employee people, Geographical Location, In the present study of 100 patients, 16% were from rural, 84% were from urban, Duration of diabetes, In this study, 43% of the patients had diabetes for a duration of 10-19 years and 38% patients for 1-9 years, According to Bhat et al²², majority of diabetic patients with cutaneous manifestations had 1-5 years of duration of diabetes (37.37%), followed by 6-10 years (24.24%). Infections were the most common dermatoses (43%), of which fungal infections were most prevalent (26%), followed by bacterial infections (12%) and viral infections (5%). This is in accordance with other studies where fungal infections were more common, as observed by Mahajan et al¹⁵ (54.68%), Bhat et al²² (34.34%) and Al-Mutairi et al²¹ (68%). Fungal agents formed largest group of cutaneous lesions and it may be because most of our patients belonged to lower socio economic group residing in slum areas where hot and humid conditions, overcrowding and decreased resistance of the body predisposes the individuals for such infections. Infections are usually common during early diabetes. This may be explained on the basis of decrease in the host defence mechanism, and decreased phagocytic activity, which is noticed immediately in uncontrolled diabetes and these changes do not require much longer time to develop unlike microangiopathy.²⁰ five patients of the 100 patients studied had viral infections, of which 4 (4%) had herpes zoster and 1 patient had (1%) verrucavulgaris. In a study conducted by Mahajan et al¹⁵, two cases of herpes zoster were reported. Similar frequencies were observed by Bhat et al²² and Al-Mutairi et al.²¹ of the 26 patients with fungal infections, majority had dermatophytoses of which 10 patients had tinea cruris, 4 had tinea corporis, 4 patients had tinea versicolor and 5 had Tinea pedis. The various candidial infections observed were, candidial vulvovaginitis in 1 patient and Candidial balanoposthitis in 1 patient. There were 1 patient of onychomycosis. Fungal infections were the commonest infections in diabetics as reported by Mahajan et al¹⁵ (21 cases), Bacterial infections, Among the 12 patients had bacterial infections, 6 patients had cellulites, 3 patients had furunculosis, 1 case each of carbuncle, abscess and folliculitis. Findings observed by Nigam et al¹⁴, in which, out of 32 patients with bacterial infections, furunculosis was the commonest (15 cases), followed by folliculitis (8 cases), cellulitis (3 cases) and two cases each of carbuncle, bacterial impetigo and multiple abscesses. In the present study, 3 patients (3%) had dermatoses associated with microangiopathy, wherein 1 patient (1%) had diabetic dermopathy, 1 patient (1%) had diabetic bullae and 1 patient had granuloma annulare (GA). Majority of the western studies report a high frequency of diabetic dermopathy (50%), as compared to 17.8% in Indian patients. Nigam et al¹⁴ reported 6 cases (3.5%) of diabetic dermopathy and 2 cases (1%) of diabetic bullae. Similarly, Mahajan et al¹⁵, in their study of 100 diabetics, found diabetic dermopathy in 6 patients and 2 cases of diabetic bullae. While a comprehensive review on the subject considers diabetic dermopathy to be the most common manifestation, we did not observe it to be so common. Skin manifestations due to diabetic microangiopathies are usually seen in chronic diabetes because the deposition of PAS - positive material within the lumina of the blood vessels occurs slowly in the disease process. Uncontrolled diabetes increases the risk of development of microangiopathy, related complications or sequelae²² and predisposes skin for various infections¹⁴ A study conducted by Raghunath et al²³ showed well controlled diabetes in majority of the patients. Random blood sugar levels, Majority of the patients had random blood sugar levels in the range of 140-200mg/dl (49%), while 29 patients (29%) had blood sugar levels of >200mg/dl.

Conclusion

This study was undertaken to know the spectrum of mucocutaneous manifestations in diabetes mellitus. Infections were the most common mucocutaneous manifestations in diabetics, followed by dermatoses most commonly associated with diabetes. Mucocutaneous manifestations are more common in patients who have overall poor glycemic control which in turn is reflected by high HbA1c value. Mucocutaneous manifestations can heighten the suspicion of a physician regarding the diagnosis of diabetes. This further helps to prevent systemic derangements by early institution of appropriate treatment.

References

1. Bilous R, Donnelly R. History of Diabetes. In: Handbook of Diabetes. 4th ed. Oxford :Wiley-Blackwell;2010;5-8
2. Dwivedi G, Dwivedi S. Sushruta-the Clinician-Teacher par Excellence. Indian J Chest Dis Allied Sci 2007; 49: 243-244
3. Tattersall RB. The History of Diabetes Mellitus. In: Holt RIG, Corkram CS, Flyvbjerg A, Goldtsein JB, editors. Textbook of Diabetes. 4th ed. Oxford:Wiley- Blackwell;2010; 3-23
4. Bennett HP. Definition, Diagnosis and Classification of Diabetes mellitus and Glucose Homeostasis. In: Kahn RC, Weir GC, King GL, Moses AC, Smith RJ, Jacobson AM , editors. Joslin's Diabetes Mellitus. 14th ed. Philadelphia: Lippincott Williams & Wilkins; 2005;332-41
5. Bilous R, Donnelly R. Introduction to Diabetes. In: Handbook of Diabetes. 4th ed. Oxford :Wiley-Blackwell;2010;3-4
6. World Health Organisation. Diabetes Mellitus: Report of a WHO Study Group. Geneva: WHO, 1985. Technical Report Series, 727.
7. Bilous R, Donnelly R. Diagnosis and classification of Diabetes. In: Handbook of Diabetes. 4th ed. Oxford :Wiley-Blackwell;2010;9-15
8. Ramachandran A, Das AK, Joshi SR, Yajnik CS, Shah S, Prasanna Kumar KM. Current Status of Diabetes in India and Need for Novel Therapeutic Agents .J Assoc Physicians India 2010;58:7-9
9. Bilous R, Donnelly R. Epidemiology and aetiology of type 2 diabetes. In: Handbook of Diabetes. 4th ed. Oxford :Wiley-Blackwell;2010;44-52
10. Bilous R, Donnelly R. Diabetes control and its measurement. In: Handbook of Diabetes. 4th ed. Oxford :Wiley-Blackwell;2010;61-7
11. Rohlfing CL, Wiedmeyer HM, Little RR, England JD, Tennill A, Goldstein DE. Defining the relationship between plasma glucose and HbA (1c): analysis of glucose profiles and HbA (1c) in the Diabetes Control and Complications Trail. Diabetes Care. 2002 Feb;25(2):275-278.
12. Jelinek JF. Cutaneous manifestations of D.M. Int J of Dermatol 1994 Sept.;33 (90):605-617.
13. Seghal S, Sanker P. Some aspects of skin disease and DM. Indian J Dermatol Venereol Leprol; 1965;31(6):264-269.
14. Nigam PK, Pande S. Pattern of dermatoses in diabetics. Indian J Dermatol Venereol Leprol 2003; 69:83-5
15. Mahajan S, Koranne RV, Sharma SK. Cutaneous manifestation of diabetes mellitus. Indian J Dermatol Venereol Leprol 2003;69:105-8
16. Sarkany RPE, Breathnach SM, Morris AAM, Weismann K, Flynn A. Metabolic and nutritional disorders. In: Burns t, Breathnach S, Cox N, Griffiths C (editors). Rook's Textbook of Dermatology. 8th ed. 2010: 59.77- 59.80
17. Lithner F. Cutaneous erythema with or without necrosis localized to legs and feet – a lesion in elderly diabetes. Acta Med Scand 1976;199(3):203-209.

18. Oimomi M, Maeda Y, Hata F, Nishimoto S, Kitamura Y, Matsumoto S et al. Glycosylation levels of nail proteins in diabetic patients with retinopathy and neuropathy. *Kobe J Med Sci* 31:183-188, 1985
19. Sawhney M, Talwar OP, Tutakne MA, Rajpathak SD. Diabetic dermoangiopathy: A Clinico-pathological correlation. *Indian J Dermatol Venereol Leprol.* 1992;58:172-178.
20. Rao S. Pai G. Cutaneous manifestations of diabetes mellitus. *Indian J Dermatol Venerol Leprol*; 1997;63;4:232-34
21. Al-Mutari N, Zaki A, Sharma KA, Al-Sheltawi M. Cutaneous Manifestations in Diabetes Mellitus. *Med Princ Pract.*2006; 15:427-30
22. Bhat JY, Gupta V, Kudyar PR. Cutaneous manifestations of diabetes mellitus. *Int J Diab Dev Ctries*, 2006;26(4):152-54
23. Raghunatha S, Anitha B, Inamdar AC, Palit A, Devarmani SS. Cutaneous disorders in 500 diabetic patients attending Diabetic clinic. *Indian J Dermatol*, 2011;56(2):160-64