www.jmscr.igmpublication.org
Impact Factor (SJIF): 6.379
Index Copernicus Value: 71.58
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossrefDOI: https://dx.doi.org/10.18535/jmscr/v6i7.122

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

**Original Research Article**

# Cutaneous manifestations in patients with diabetes mellitus in a tertiary care hospital at Bihar, India: An Observational Study

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**Abstract**
**Background:** *Almost all diabetic patients eventually develop skin complications from the long-term effects of diabetes mellitus on the microcirculation and on skin collagen. Cutaneous infections are more common in type 2 diabetes, whereas autoimmune-related lesions are more common in type 1.*
**Methodology:** *This observational study was conducted with patients in the Diabetic OPD of a tertiary care teaching hospital in Eastern India from January 2016 to December 2016. Two hundred patients satisfying the diagnostic criteria for diabetes were taken. A detailed history was elicited in each case with particular reference to cutaneous complaints and including details regarding duration, history of evolution, progression and treatment modalites, if any.*
**Results:** *Of the study population 178 (89%) were cases of type 2 diabetes, 19 (9.5%) type 1 diabetes and 03 (1.5%) were cases of gestational diabetes. Out of 200 cases, 111 (55.5%) patients had some associated cutaneous manifestations comprising 69 (62.16%) males and 42 (37.84%) females. Cutaneous infections formed the largest group of dermatoses were observed in 61 (54.95%).Among the bacterial infection which were seen in 21 (18.92%) cases, impetigo contagiosa 7 (6.31%), folliculitis and boils 6 (5.41%), and two cases of erythrasma (1.8%). Dermatophytoses were seen in 22 (19.82%) patients, comprising tinea corporis et curis 9 (8.1%), tinea unguium in 3 (2.7%), tinea pedis 8 (7.21%) and tinea incognito in 2 (1.8%). Herpes zoster was seen in 2 patients (1.8%). Dermatoses or non-infectious skin lesions were seen in 58 (52.25%) diabetic cases.*
**Conclusion:** *Diabetes mellitus can be complicated by a variety of cutaneous manifestations. As the duration of diabetes increased, the likelihood of developing skin manifestations also increases. Early referral to the dermatologist may help to detect complications of the skin in diabetes at an early stage and may prevent disability caused by these complications.*
**Keywords**: *Diabetes mellitus, Cutaneous manifestations, Fungal infections, Dermatophytic infections, Dermatoses.*

## Introduction

Diabetes mellitus, more simply called diabetes, is a chronic condition that occurs when there are raised levels of glucose in the blood because the body cannot produce any or enough of the hormone insulin or use insulin effectively. Type 1 diabetes is caused by an autoimmune reaction where the body's immune system attacks the insulin-producing beta cells in the islets of the pancreas gland. Type 2 diabetes is the most common type of diabetes, accounting for around 90% of all cases of diabetes. In type 2 diabetes, hyperglycaemia is the result of an inadequate production of insulin and inability of the body to respond fully to insulin, defined as insulin resistance.[2,3] Global estimates of type 2 diabetics in the year 2030 is likely to be 552 million. The International Diabetes Federation (IDF) documents the total number of diabetic subjects to be around 61.3 million in India and this is further set to raise to 101.2 million by the year 2030.[4]

It exhibits a variety of multisystem complications involving the blood vessels, skin, eye, kidney, and the nervous system during the course of the disease process. Abnormal carbohydrate metabolism, other altered metabolic pathways, atherosclerosis, microangiopathy, neurone degeneration, and impaired host mechanisms all play roles.[5] More than one third of diabetic patients have some type of dermatologic manifestations during the course of their chronic disease.[6] Abnormal carbohydrate metabolism, atherosclerosis, microangiopathy, neuron degeneration and impaired host mechanism all play roles in the pathogenesis of cutaneous complications.[7]

There no epidemiologic data related to skin disorders in diabetics reported from Eastern India especially from Bihar. This study was designed to analyze the prevalence and pattern of skin disorders among diabetic patients from this region.

## Materials & Methods

This observational study was conducted with patients in the Diabetic OPD of a tertiary care teaching hospital in Eastern India from January 2016 to December 2016. Two hundred patients satisfying the diagnostic criteria for diabetes were taken. The data were collected prospectively and systematically in a pre-established proforma after an informed written consent was obtained from all subjects. History, including age, sex, type of diabetes, duration, complications and treatment modalities were noted. All the patients were subjected to complete and thorough dermatological examination. A detailed history was elicited in each case with particular reference to cutaneous complaints and including details regarding duration, history of evolution, progression and treatment modalites, if any. Apart from routine haematological investigations, fasting and post prandial blood sugar levels were done in all the patients. Glycosylated Haemoglobin levels were done in patients by Ion exchange resin method. The fungal infections were confirmed by wet mount in 10%-40% Potassium hydroxide solution. Bacterial infections were confirmed by smear examination in gram stain and bacterial culture. Serum lipid profile, serum creatinine, and fundus examination were done to detect complications. Relevant microbiological and histopathological investigations were done wherever necessary to confirm the clinical diagnosis. Findings were recorded and results obtained were tabulated and statistically analyzed.

## Results

Of the study population 178 (89%) were cases of type 2 diabetes, 19 (9.5%) type 1 diabetes and 03 (1.5%) were cases of gestational diabetes. Of the 178 patients with NIDDM 117 (65.73%) were males and 61 (34.67%) were females and of the 19 of type 1 diabetes patients 13 (68.42%) were males and 6 (31.58%) were females. The age varied from 11 to 84 years, mean age being 48.7±7.9 years. The duration of diabetes was 1-10

years in 164 patients (82%) and 19 (9.5%) had >10 years of diabetes. Seventeen patients (8.5%) were newly diagnosed as diabetics. The maximum number of patients was in the age group of 41 to 60 years 93 (46.5%) followed by 20 to 40 years 68 (34%). In diabetic cases, the mean body mass index was found to be 26.1±3.5 (mean ± SD). Out of 200 cases, 111 (55.5%) patients had some associated cutaneous manifestations comprising 69 (62.16%) males and 42 (37.84%) females [Table 1].

**Table 1:** Demographic and clinical characteristics of diabetic patients [n=200]

| Characteristics | No. of patients | Percentage/ Mean±SD |
|---|---|---|
| Type 1 diabetes | 19 | 9.5% |
| Males | 13 | 68.42% |
| Females | 6 | 9.5% |
| Type 2 diabetes | 178 | 89% |
| Males | 117 | 65.73% |
| Females | 61 | 34.67% |
| Gestational diabetes | 03 | 1.5% |
| Mean age [years] | 200 | 48.7±7.9 |
| Age groups [years] | | |
| < 20 | 9 | 4.5% |
| 20-40 | 68 | 34% |
| 41-60 | 93 | 46.5% |
| >60 | 30 | 15% |
| Duration of diabetes | | |
| Newly onset | 17 | 8.5 |
| 1-10 yrs | 164 | 82 |
| >10 years | 19 | 9.5 |
| Mean body mass index | 200 | 26.1±3.5 |
| Cutaneous manifestations | 111 | 55.5% |
| Males | 69 | 62.16% |
| Females | 42 | 37.84% |
| Cutaneous manifestations with duration of diabetes | | |
| < 1 year | 6 | 5.41% |
| 1-5 years | 34 | 30.63% |
| 6-10 years | 24 | 21.62% |
| > 10 years | 47 | 42.34% |
| Associated disorders with cutaneous manifestations | | |
| Hypertension | 33 | 29.73% |
| Nephropathy | 4 | 3.60% |
| Neuropathy | 5 | 4.50% |
| Retinopathy | 4 | 3.60% |
| HbA1c with cutaneous manifestations | | |
| Controlled | 60 | 54.05% |
| Uncontrolled | 51 | 45.95% |

The cutaneous manifestations were most prevalent in the age group of 41- 60 years. The majority of patients 34 (30.63%) with cutaneous manifestations were having disease duration between 1-5 years, followed by 6-10 years 24 (21.62%), > 10 years 47 (42.34%) and less than one year 6 (5.41%). In diabetic patients with cutaneous manifestations, hypertension was present in 33 (29.73%), nephropathy in 4 (3.60%), neuropathy in 5 (4.50%), and retinopathy in 4 (3.60%) cases. Out of 111 patients with cutaneous manifestations, 51(45.95%) had uncontrolled and 60 (54.05%) had controlled glycosylated hemoglobin (HbA1c) level [Table 1]. Various types of skin manifestations observed are shown in Table 2.

**Table 2:** Distribution of different infective skin lesions in diabetic patients [n=111]

| Cutaneous manifestations | No. of patients | Percentage |
|---|---|---|
| Infectious skin lesions (total) | 61 | 54.95 |
| Fungal infection (total) | 36 | 32.43 |
| Candidiasis | 14 | 12.61 |
| Dermatophytic infections | 22 | 19.82 |
| Tinea corporis et curis | 9 | 8.11 |
| Tinea unguium | 3 | 2.7 |
| Tinea pedis | 8 | 7.21 |
| Tinea incognito | 2 | 1.8 |
| Bacterial infection (total) | 21 | 18.92 |
| Impetigo contagiosa | 7 | 6.31 |
| Boils | 6 | 5.41 |
| Folliculitis | 6 | 5.41 |
| Erythrasma | 2 | 1.8 |
| Infestation (Scabies) | 01 | 0.9 |
| Viral infection | 02 | 1.8 |

Cutaneous infections formed the largest group of dermatoses were observed in 61 (54.95%). Among the bacterial infection which were seen in 21 (18.92%) cases, impetigo contagiosa 7 (6.31%), folliculitis and boils 6 (5.41%), and two cases of erythrasma (1.8%). Dermatophytoses [Figure 1] were seen in 22 (19.82%) patients, comprising tinea corporis et curis 9 (8.1%), tinea unguium in 3 (2.7%), tinea pedis 8 (7.21%) and tinea incognito in 2 (1.8%). Herpes zoster was seen in 2 patients (1.8%) [Table 2].

**Table 3:** Distribution of different non-infective skin lesions in diabetic patients [n=111]

| Cutaneous manifestations | No. of patients | Percentage |
|---|---|---|
| Non-infectious skin lesions (total) | 58 | 52.25 |
| Xerosis | 16 | 14.41 |
| Lipodystrophy | 4 | 3.6 |
| Skin rash | 2 | 1.8 |
| Hyperpigmentation | 2 | 1.8 |
| Lichen planus | 1 | 0.9 |
| Vitiligo | 2 | 1.8 |
| Prurigo nodularis | 2 | 1.8 |
| Xanthoma | 4 | 3.6 |
| Acanthosis nigricans | 7 | 6.31 |
| Thickening of skin | 2 | 1.8 |
| Bullous diabeticorum | 1 | 0.9 |
| Psoriasis | 1 | 0.9 |
| Granuloma annulare | 0 | 0 |
| Sclerederma diabeticorum | 0 | 0 |
| Rubeosis facei | 2 | 1.8 |
| Epidermal Necrolysis/Stevens Johnson Syndrome | 0 | 0 |
| Onychodystrophy | 3 | 2.7 |
| Periungual telangectasias | 1 | 0.9 |
| Seborrheic keratosis | 4 | 3.6 |
| Eczema | 3 | 2.7 |
| Melasma | 0 | 0 |
| Keloid | 1 | 0.9 |
| Cutaneous amyloidosis | 0 | 0 |

Dermatoses or non-infectious skin lesions were seen in 58 (52.25%) diabetic cases [Table 3]. It was found that xerosis (14.41%), acanthosis nigricans (6.31%), seborrheic keratosis (3.6%), lipodystrophy (3.6%), xanthoma [Figure 2] (3.6%), skin rash (1.8%), and hyperpigmentation (1.8%) were reported as non infectious skin manifestations in patients with diabetes mellitus [Table 3]. However, the pattern of lesions was different in Type 1 and Type 2 diabetics. Nine patients out of the 19 (47.37%) type 1 diabetics demonstrated skin lesions, the commonest being diabetic xerosis, infections and diabetic hand. In Type 2 diabetics 101 (90.99%) showed skin lesions followed by one patient (0.9%) in gestational diabetes. Dermatoses, having a possible association with diabetes mellitus were the first to appear, followed by cutaneous infections. Dermatoses, having a strong association with diabetes mellitus were found to occur in patients with a longer duration of diabetes.

**Figure 1:** Dermatophytic infections

**Figure 2:** Eruptive xanthomas

**Figure 3:** Xerosis in diabetic subjects

**Discussion**

The skin is affected by both the acute metabolic derangements and the chronic degenerative complications of diabetes.[5] 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.[8] The association of certain skin diseases with diabetes mellitus has been fairly well recognized with an incidence rate ranging from 11.4 to 71%.[9-11]

In our study, the majority of patients were between 41- 50 years and the mean age of patients was 48.7±7.9 years. Females outnumbered males and female: male ratio was 1.86:1. The duration of diabetes was 1-10 years in 164 patients (82%) and 19 (9.5%) had >10 years of diabetes. Seventeen patients (8.5%) were newly diagnosed as diabetics. In Phulari YJ et al study[12], majority 50.58% were <5 years, 27.05% in 6 to 10 years, 11.76% in 16 to 20 years and 10.85% in 11 to 15 years. Study by Kumar et al[13] showed that the duration of diabetes was < 10 years in 30 patients, 17 had 11-20 years and 3 had > 20 years of diabetes.

In the present study the commonest cutaneous feature of diabetes was cutaneous infections (Table 2), seen in 61 (54.95%) patients and dermatophytosis seen in 22 (19.82%) patients. Among the bacterial infection which were seen in 21 (18.92%) cases, impetigo contagiosa 7 (6.31%), folliculitis and boils 6 (5.41%), and two cases of erythrasma (1.8%). Dermatophytoses were seen in 22 (19.82%) patients, comprising tinea corporis et curis 9 (8.1%), tinea unguium in 3 (2.7%), tinea pedis 8 (7.21%) and tinea incognito in 2 (1.8%). Herpes zoster was seen in 2 patients (1.8%). Chatterjee N et al[14] showed about 73.9% of diabetic patients had one or more cutaneous manifestations. Study by Timshina DK et al[15] revealed cutaneous infections formed the largest group of dermatoses in both the cases and controls, and were observed in 94 (41.9%) cases and 42 (18.8%) controls. Study by Mahajan S et al[5] reported that cutaneous infections bacterial and fungal, constituted the largest group affecting 35 (54.69%). Of the 64 cases having cutaneous manifestations pruritus was second most common manifestation (15.62%) in the present study. Most documented studies have shown the incidence of cutaneous disorders associated with diabetes to be between 30% and 71. [16-18] In the present study, infections formed the largest group (54.95). Xerosis was the second most common manifestation (14.41%). Rao and Pai found that pruritus was the main presenting symptom and was noted in 60.23% patients in their series.[19]

Skin disorders will be present in 79.2% of people with diabetes.[20] A study of 750 patients with diabetes found that the most common skin manifestations were cutaneous infections (47.5%), xerosis (26.4%), and inflammatory skin diseases (20.7%).[20] The high incidence of skin manifestations in diabetes has been reported by Nigam and Pande (61%)[10] , Mahajan et al (64%)[5], and Wahid and Kanjee (82%)[11], whereas lower incidence has been reported by other workers.[21] The female predominance was seen in our study as reported by Mahajan et al[5] and Romano et al[18].

Diabetic dermopathy is the most common cutaneous marker of diabetes mellitus presenting as single or multiple well demarcated brown atrophic macules, predominantly on the shins.[14]

Study by Chatterjee N et al[14] failed to show correlation between good metabolic control and

skin lesions. However the mean HbA1C level was higher in patients with infective lesions (8.7 ± 1.4 in contrast to 7.2 ± 1.3). Study by Chatterjee N[14] revealed 73.9% of diabetic patients had one or more cutaneous manifestations. Mahajan et al.[5], reported cutaneous infections in 54.69% of diabetics in their study group.

Acanthosis nigricans is likely the most readily recognized skin manifestation of diabetes (3). It is present in up to 74% of obese adult patients and can be predictive of the existence of hyperinsulinemia.[22] Raised levels of insulin act on insulin-like growth factor receptors leading to the development of acanthosis nigricans.[23] The proportion of acanthosis nigricans among the diabetics in the study is similar to studies done on Indian patients. [24-26] Grandhe et al[27] found acanthosis nigricans to be an independent cutaneous marker of type 2 diabetes mellitus.

Diabetic Dermopathy presents as small (<1cm), well-demarcated, atrophic depressions, macules, or papules on the pretibia and is considered to be a sign of insulin resistance. Diabetic dermopathy probably represents post-traumatic atrophy and post-inflammatory hyperpigmentation in poorly vascularized skin.[28] Eruptive xanthoma (EX) [Figure 2] presents on the buttocks, elbows, and knees as sudden onset crops of yellow papules with an erythematous base. It is rare and occurs more often in patients with poorly controlled type 2 diabetes.[29]

Stevens-Johnson syndrome is a rare mucocutaneous necrotizing condition. The dipeptidyl peptidase-4 inhibitor sitagliptin has been associated with cases of Stevens-Johnson Syndrome.[30] It could present with fever, headache, rhinitis, cough, malaise, burning eyes, and dysphagia.[30] Vitiligo affects 0.3–0.5% of world population, making it the most common depigmenting disorder. A 2009 study of 50 patients with type 1 diabetes reported that 4% of subjects had vitiligo.[5] Vitiligo has been associated with both type 1 and type 2 diabetes mellitus and there is an increased association of vitiligo with a proven or presumed autoimmune disease.[15, 31] Patients with vitiligo, lichen planus, and cutaneous perforating dermatosis are reported to have an increased incidence of abnormal glucose tolerance or frank diabetes mellitus.[32] Xerosis [Figure 3] is another name for dry skin. It is the second most common skin manifestation in people with diabetes.

Yosipovitch et al.[33] and Sawhney et al.[34] observed that majority of the patients with cutaneous lesions in their respective studies were under poor glycemic control. In Sanad et al[35] study, cutaneous infections included fungal (22%), bacterial (16%), and viral (2%) infections. Diabetic dermopathy probably represents post-traumatic atrophy and post-inflammatory hyperpigmentation in poorly vascularized skin.[28]

In the present study diabetic patients with cutaneous manifestations, hypertension was present in 33 (29.73%), nephropathy in 4 (3.60%), neuropathy in 5 (4.50%), and retinopathy in 4 (3.60%) cases. High prevalence of systemic complications has been reported in diabetic patients with cutaneous involvement as compared to diabetics without cutaneous manifestations.[25, 28] According to an Indian study in 2008, no correlation was demonstrated between glucose control and dermatologic manifestations.[15] But an Iranian study[36] as well as a study by Rayfield et al[37] showed definite relationship between foot ulcers and fungal infections with HbA1C levels. Study by Ghosh K et al[38] showed that uncontrolled DM or higher HB1AC is associated with diabetic bulla, scleredema, lichen planus and signs of insulin resistance. There is no association with any kind of skin manifestations and microangiopathic complications though often cited as an etiopathogenic factor was found.

## Conclusion

Skin manifestations are seen frequently in diabetes mellitus and sometimes may signal the onset of this disorder. Without the control of diabetes mellitus, the mucocutaneous manifestations are often intractable. The frequency of cutaneous infections as well as diabetes-related dermatoses

was higher among the diabetics than among nondiabetics. Patients with poorly controlled diabetes had more number of cutaneous infections and diabetes associated dermatoses. Impaired diabetic control as evidenced by higher HbA1C levels was found among patients with infections. To conclude, diabetes mellitus involves the skin quite often and whenever patients present with multiple skin manifestations their diabetic status should be checked.

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