

An Observational Study of Cutaneous Manifestations Associated with Diabetes Mellitus

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Abstract:

Background and Aim: The pathophysiology of diabetes mellitus and its effects on the human body have been well analysed over the years. Nevertheless, the skin, which is the biggest organ in the body, has been given minimal attention. The purpose of this study was to determine the various skin symptoms observed in diabetic patients.

Material and Methods: A cohort of 180 diabetes patients with cutaneous symptoms, who visited the skin outpatient department (OPD) at a prestigious teaching hospital in India over a period of 1 year, were chosen by a random selection process. A comprehensive evaluation was conducted, which included a thorough analysis of the patient's medical history, a detailed physical examination, and an assessment of the involvement of the skin and mucous membranes. The diagnosis of Diabetes Mellitus was established through the assessment of urine sugar and blood sugar levels. The diagnosis of diabetes mellitus was made according to the criteria established by the national diabetic data group. Urine and blood sugar levels were assessed in all instances.

Results: A total of 53 individuals fell into the age category of 40 years, accounting for 28% of the sample. Among the 180 instances, 61.1% were male patients and 38.8% were female patients. A total of 68 cases were diagnosed with various fungal diseases, including Tinea corporis, Tinea cruris, Tinea Versicolor, Candidal intertrigo, Candidal vulvovaginitis, Candidal balanoposthitis, and oral candidiasis. These cases accounted for 37.7% of the total. Within this investigation, there were 22 instances of bacterial infections. Observations revealed symptoms such as excessive urination (polyurea), increased appetite (polyphagia), excessive thirst (polydipsia), weight loss, widespread itching (generalised pruritus), painful sensation, and itching in the genital area.

Conclusion: Diabetes mellitus is a prevalent medical condition that affects various medical specialties due to its wide range of clinical symptoms. Even the skin is not exempt, with around one third of patients with diabetes predicted to experience cutaneous alterations.

Keywords: Cutaneous manifestations, Diabetes mellitus, Polyurea, Tinea corporis.

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Introduction

Diabetes mellitus is a significant global health challenge due to its rising incidence and the intricate nature of its systemic and local symptoms. Currently, diabetes impacts about 500 million individuals worldwide, accounting for a prevalence of over 10.5% among adults. The manifestations of diabetes are diverse, with a significant number occurring at the skin level. Therefore, the dermatologist plays a crucial role in identifying these connections. Conditions such as acanthosis nigricans, diabetic dermopathy, lipoid necrobiosis, bacterial and fungal infections, and skin xerosis are commonly linked to diabetes and often occur before its diagnosis. [1,2] Diabetes mellitus is a prevalent medical illness that affects various

medical specialties due to its wide range of clinical symptoms. It is believed that up to one-third of people with diabetes mellitus experience changes in their skin. Put simply, when applying the most inclusive definition, all individuals with diabetes will experience cutaneous signs of this condition. [3] The cutaneous symptoms observed in individuals with diabetes are equally present in those without diabetes. The precise mechanism behind most cutaneous manifestations linked with diabetes mellitus remains mostly understood. Currently, there is a significant emphasis on a shared factor among all forms of diabetes, which is Hyperglycemia. However, the primary elements that likely contribute to the development of

cutaneous manifestations include hyperglycemia, macro and microangiopathy, and neuropathy. [3] There is a scarcity of Indian studies regarding the skin conditions related to diabetes mellitus. Therefore, this thesis aims to investigate the cutaneous manifestations associated with diabetes mellitus in patients who visit the skin outpatient department at a prestigious teaching hospital in India. The objective of this study was to determine the various skin symptoms observed in diabetic patients.

Material and Methods

A sample of 180 diabetes patients with skin symptoms, who visited the skin outpatient department (OPD) at a prestigious teaching hospital in India for a period of 1 year, were chosen in a random manner. Each case was thoroughly evaluated by a comprehensive analysis of medical records, a meticulous physical examination, and assessment of any skin or mucous membrane manifestations. The diagnosis of diabetes mellitus was verified through the assessment of urine sugar and blood sugar levels.

The investigations conducted included routine blood examination, such as HB% (haemoglobin percentage), total count, differential count, and ESR (erythrocyte sedimentation rate) in all cases. Urine tests were performed to check for sugar and albumin in all cases. Blood sugar estimation, either fasting blood sugar or random blood sugar, was conducted in all cases. Additionally, direct examination of scrapping taken from affected areas was performed to detect fungal elements in dermatophytosis, and : Pus and discharge samples were collected for gramme staining to identify the organism. In chosen cases, culture and sensitivity tests were performed to examine for bacterial and fungal presence. Additionally, skin lesion biopsies were conducted at the affected site in selected cases.

Statistical analysis: The collected data was consolidated and inputted into a spread sheet software (Microsoft Excel 2007) and subsequently transferred to the data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). Quantitative variables were characterised using either means and standard deviations or medians and interquartile ranges, depending on their distribution. The qualitative factors were displayed as counts and percentages. The confidence level and level of significance for all tests were established at 95% and 5% respectively.

Results

According to Table 1, there were 53 patients who were between the ages of 40 years, making up 28% of the total. The two patients with the lowest age were both 16 years old. According to Table 2, among the 180 cases, 61.1% were male patients and 38.8% were female patients.

A total of 68 cases were diagnosed with various fungal diseases, including Tinea corporis, Tinea cruris, Tinea Versicolor, Candidal intertrigo, Candidal vulvovaginitis, Candidal balanoposthitis, and oral candidiasis. These cases accounted for 37.7% of the total. Within this investigation, a total of 22 cases exhibited bacterial infections, including carbuncle, folliculitis, furunculosis, and palmar abscess. These cases accounted for 12.2% of the overall total, as indicated in Table 3. According to Table 3 and 4, there were 30 cases of generalised pruritus, accounting for 16.6% of the total cases.

Thirty instances of acrochordons were observed, with 11 cases being linked to generalised pruritus, 5 cases associated with Tinea cruris, 4 cases solely presenting acrochordons, 3 cases of skin tags having associated monilial intertrigo, and one case each associated with infected eczema, furuncle, folliculitis, tinea pedis, and psoriasis, respectively. Lichen planus was observed in instances of both genders, accounting for 5% of the total cases. According to Table 3, three instances of psoriasis were identified, with one of those cases having accompanying skin tags. Therefore, a mere 3% of instances were observed. The prevalence of viral infection accounts for 2% of the overall cases.

Observations revealed symptoms such as excessive urination (polyuria), increased appetite (polyphagia), excessive thirst (polydipsia), weight loss, widespread itching (generalised pruritus), painful sensation, and itching in the genital area. All diabetic patients, except for 14 individuals, exhibited the aforementioned symptoms. These 14 patients were diagnosed with diabetes based on skin symptomatology.

Among the 180 cases analysed, 18 patients only received insulin therapy, while the remaining 140 patients were prescribed hypoglycemic medications. The remaining 22 patients identified throughout the investigations have been sent to the diabetes clinic for additional treatment and care. The Gram's staining procedure was conducted in 60 cases as part of the current study. Out of a total of 60 instances, 40 cases were diagnosed with candidal or monilial infection using gram's staining, while the remaining 20 cases were found to have bacterial infection.

Table 1: Age wise distribution of the cases

Age (in years)	Number of cases	Percentage (%)
10-20	4	2.22
21-30	14	7.77
31-40	35	19.4
41-50	67	37.2
51-60	42	23.3
61-70	36	20
71-80	2	1.11

Table 2: Gender wise distribution of the cases

Gender	Number of cases	Percentage (%)
Male	110	61.1
Female	70	38.8
Total	180	100

Table 3: Cutaneous manifestations associated with diabetes

Disease associated with diabetes	Number of cases	Percentage (%)
Fungal	66	36.6
Bacterial	20	11.11
Acrochordans	30	16.6
Generalized pruritus	30	16.6
Lichen planus	30	16.6
Psoriasis	5	2.7
Polymorphic light eruption	5	2.7
Pruritus ani	5	2.7
Vitiligo	4	2.2
Infected eczema	4	2.2
Kyrle's disease	3	1.6
Parasitic infection (scabies)	3	1.6
Viral infection	4	2.2
Lichen Simplex Chronicus	4	2.2
Photodermatitis	3	1.6
Lipoatrophy (Localized)	2	1.11
Prurigo simplex	2	1.11
Bullous disease	2	1.11

Discussion

In most cases, cutaneous manifestations of diabetes mellitus occur subsequent to the development of the underlying disease; however, they can manifest concurrently with its initiation or even many years prior to diabetes. While the precise mechanisms underlying numerous skin conditions associated with diabetes are still unknown, others have been linked to abnormal carbohydrate metabolism, altered metabolic pathways, atherosclerosis, microangiopathy, neuron degeneration, and compromised host mechanisms. [4]

A minimum of 30% of patients diagnosed with diabetes mellitus exhibited an association with cutaneous involvement of some kind throughout the duration of their chronic condition. [5,6] According to the majority of published research, the prevalence of cutaneous disorders related to diabetes ranges from 30% to 71%. 7.8 73.9 percent of diabetic patients in the present study exhibited one or more cutaneous manifestations. Skin lesions with a weak to strong association with diabetes,

infections (bacterial, fungal), cutaneous manifestations of diabetic complications (microangiopathy, neuropathy), and skin reactions to diabetic treatment (sulphonylureas or insulin) comprise the four categories of diabetic cutaneous manifestations. [9] Malay cutaneous infections were reported by 54.69% of diabetics in the study cohort of Mahajan et al. [8]

The majority of patients (72% in the present study) had cutaneous manifestations associated with diabetes and were 41 years of age or older. Anand LC et al. made a nearly identical observation (74% in their study). [4] Males exhibited a higher sex incidence rate (62%) compared to females (38%), according to research conducted by Thomas Georges et al. [10] Similar findings were observed in the current series, which revealed 38% females and 62% males.

The current series found that 12.5% of all diabetic patients had bacterial infections, which is consistent with the findings of George T. et al. [10]

Therefore, it is recommended that patients with recurrent chronic bacterial infections undergo urinary and blood sugar testing. In the present investigation, fungal infections were identified in 38 cases (68 cases), representing a major group of concomitant manifestations associated with diabetes. George T et al. reported a comparable high incidence of fungal infections (44%), while Anand LC et al. identified fungal infections in 35% of the cases. [4,10] Viral infections affected two percent of the patients in the present study. According to Brown et al., diabetics have a high incidence of Herpes zoster accompanied by postherpetic neuralgia. However, Rogozzino and Melton et al. discovered that 15% of diabetics had Herpes zoster infection and concluded that the two conditions do not interact as risk factors for diabetes mellitus. [11,12] Jelinek et al. have identified a heightened prevalence of oral lichen planus among individuals with diabetes. [13] of the cases of lichen planus in this series did not involve buccal lesions (6%). According to Lisi et al., lichen planus is linked to a metabolic alteration and an immunological defect, respectively. At this time, the hypothesis that skin tags indicate diabetes lacks scientific evidence. Theoretically, the association is postulated to exist between fibroblast growth factor and diabetes, with insulin serving to enhance the impact of this factor. Additionally, Huntley AC et al. established a correlation between diabetes and numerous, sizable hyperpigmented tags. [14]

Skin changes can be induced by constant hyperglycemia through a variety of mechanisms. Cells can be impacted by increased plasma glucose levels in two ways: directly, and via advanced glycosylation end-products (AGEs). Hyperglycemia has the potential to induce direct effects on the activity of fibroblasts and keratinocytes via modifications in protein synthesis, proliferation, and migration. Vasodilation dysfunction can also transpire due to the inhibition of nitric oxide molecules. In addition, the overregulation of sorbitol damages mitochondria, which ultimately results in the emission of reactive oxygen species. [3,4,15] AGEs are generated through nonenzymatic reactions involving glucose and other molecules. These AGEs subsequently bind to particular receptors and stimulate the production of pro-inflammatory cytokines. Furthermore, AGEs have the ability to generate free radicals, which results in oxidative stress. Conversely, specific interactions between advanced glycation end products (AGEs) and epidermal growth factor (EGF) or collagen type 1 can inhibit integument regeneration. [5,17] Non-enzymatic glycosylation of numerous structural and regulatory proteins, including collagen, occurs in response to hyperglycemia. Non-enzymatic glycosylation is a natural consequence of ageing; however, diabetes significantly accelerates this

process. The formation of advanced glycosylation end products, which result from non-enzymatic glycosylation, is accountable for the reduction in acid solubility and enzymatic degradation of collagen in the epidermis. It is believed that changes, including impaired joint mobility and thickened epidermis, manifest as a direct consequence of the buildup of advanced glycosylation end products in individuals with diabetes. The presence of advanced glycosylation end products in the epidermis has been found to be significantly associated with microvascular complications of diabetes, including retinopathy and nephropathy, according to studies. [18-20]

The current investigation observed 2% of the total number of patients with vitiligo, both of whom were over the age of 40. A strong correlation between vitiligo and diabetes mellitus has been identified. Vitiligo was identified in 4.8% of diabetics by Dawber et al. A reported incidence of vitiligo in patients with late-onset diabetes ranges from 4.5% to 7.7%. [21] Although Hajini GH et al. identified this condition in both insulin-dependent and non-insulin-dependent forms of diabetes, it is typically observed in patients over the age of 40. [22] The current investigation identified 2% of the cases as infected eczema, with Lichen simplex chronicus accounting for 4% of the total cases. Anand LC et al. argue that attributing eczema to an aberrant carbohydrate metabolism is not possible. [4] Carbohydrate intolerance must be given significant consideration in the treatment of any refractory eczema that is resistant to treatment and for which a definitive etiological factor has not been identified, even if it is merely an association.

At the time of the case studies in the present investigation, the following symptoms were frequently observed: polyurea, polyphagia, polydipsia, weight loss, generalized pruritus or itching, pain, and in 5% of cases, itching over the genitalia. George T et al. identified ten prevalent symptoms associated with diabetes at the time of diagnosis: polyurea (50%), polyphagia (48%), polydipsia (44%), weight loss (18%), lesional pain (4%), and irritation over the genitalia (2%). The increased prevalence of symptoms observed in the current study could potentially be attributed to the inclusion of long-standing diabetic patients, whereas the reduced incidence of symptoms reported by George T et al. could be attributed to patients with recent onset of diabetes.

Gram's staining was performed on sixty cases of candidial and bacterial infections in the present study; all thirty-four cases contained gram-positive pathogens. Greenwood et al. found that diabetics have a higher incidence of staphylococcus aureus-caused lesions compared to non-diabetics. This disparity may indicate a bacterial flora imbalance that favours the proliferation of potentially

pathogenic gram-positive cocci. [23] Additionally, diabetics have a diminished bactericidal activity against *Staphylococcus aureus* and *E. coli*, according to Rayfeild et al. [24]

No structural alterations were detected in the adjacent healthy epidermis of any of the patients for whom a biopsy was performed. Histopathological changes, including macro and microangiopathies, have been documented by authors such as Jelinek, Huntley AC, George T et al. in both normal diabetic epidermis and in cases of non-insulimal diabetic bullae (NLD). [10,13]

A study conducted in India in 2008 found no evidence to support a correlation between glucose control and dermatologic manifestations. [25] However, both an Iranian study [26] and a Rayfield study [24] demonstrated a clear correlation between fungal infections and foot ulcers in relation to HbA1C levels.

Conclusion

Diabetes mellitus is a prevalent medical condition whose spectrum of clinical manifestations encompasses nearly every medical specialty. Skin changes are not an exception; it is estimated that as many as one-third of diabetic patients have cutaneous alterations. In actuality, skin manifestations hold significant significance as they frequently serve as initial indicators of disease progression or diagnosis.

Physicians ought to possess knowledge regarding the cutaneous manifestations associated with diabetes mellitus. Ignorance regarding the cutaneous manifestations associated with diabetes or inadequate treatment may exacerbate the condition. Detection and treatment of prevalent skin manifestations associated with diabetes in a timely manner will prevent treatment-related complications and inefficacy.

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