Patterns of dermatological disorders among diabetics

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Abstract

Diabetes Mellitus is a common metabolic disorder associated with significant dermatological alterations. This study was set out to demonstrate the pattern of the various dermatological disorders seen among diabetic population in Obafemi Awolowo University Teaching Hospitals Complex Ile Ife, a tertiary health care institution in south west Nigeria. Infective skin conditions appear to occur with greater frequency compared to the non-infective dermatoses and poor glycaemic control seems to be the most significant predictor of the presence of such skin lesions (p<0.001).

Among diverse numbers of cutaneous lesions seen in this study, superficial fungal infections accounted for the highest prevalence and was seen in 35.4%. Pruritus ranked next with a prevalence of 16.7%. Others include Diabetic dermopathy (14.8%), acanthosis nigricans (4.9%), and Diabetic thick skin seen in 4% etc. The overall prevalence of cutaneous lesions in this study was 73%.

Introduction

Diabetes mellitus is the most common metabolic disorder of man that affects all socioeconomic strata and age groups. Frequency in the general population is between 2-6% while its incidence is known to be gradually increasing. [1] The disease affects approximately 60 million people globally. [2] However, between 1958 and 1993 the number of individuals diagnosed with diabetes mellitus increased fivefold. [3] It has been estimated by the World Health Organization (WHO) that the incidence will rise to 300 million by the year 2025.

The rise in the prevalence of diabetes mellitus and other non-communicable diseases in Africa is due to increasing aging of the population and westernization of the life style.[4] Type 2 diabetes (T2DM) is the predominant form, yet, a classification problem persists for a proportion of patients. [5] [6]

Interest in the skin manifestations of diabetic microangiopathy started in 1964 when Bauer et al [7] demonstrated periodic acid-schiff positive capillary basement membrane thickening (CBMT) in necrobiosis lipoidica diabeticorum (NLD) which was similar to the changes seen in diabetic microangiopathy in dermopathic lesion by Binkley [8] and in granuloma annulare. Other workers have also suggested that the underlying pathology of bullosis diabeticorum and rubeosis may be microangiopathy. [9] [10] [11]

A relationship exists between diabetes mellitus and a series of cutaneous disorders. Diabetes mellitus related dermatoses usually occur when the underlying disease had already developed, however some skin disorders may herald or occur simultaneously with or even precede the underlying disease.[12] Some of these dermatoses (acanthosis nigricans, purpuric and pigmented capillaritis) are markers of macrovascular complications. These disorders including xerosis, dupytren's disease are also more frequently associated with microangiopathy in T2DM. Other skin diseases such as alopecia areata and vitiligo are markers of autoimmunity in type I diabetes. [13]

At least 30% of diabetic patients have skin alterations which are related to diabetes mellitus, however some authors believe that the percentage may climb to 100% primarily due to the chronic nature of the disease. [14] [15] [16] In 1995, Onunu et al [17] studied the prevalence of cutaneous lesions among 250 diabetics and they put this at 63.2%.They found that the prevalence of cutaneous fungal infections, bacterial infections, foot ulcers, limb gangrene, amputated limbs and bullosis diabeticorum were significantly high in diabetic population. Necrobiosis lipoidica diabeticorum, diabetic dermopathy, insulin dystrophy, granuloma annulare, discoid lupus erythematosus were also seen.

There are many skin disorders that are readily recognizable as markers of diabetes mellitus. Some of these disorders occur as a direct sequelae of diabetes mellitus or its major vascular complications, and neuropathy. Others are related to the impaired immunity seen in diabetes, whereas some occur as a consequence of the anti-diabetic treatment.

Aims of the Work

1. To determine the prevalence and pattern of skin lesions among diabetic patients attending outpatient clinic at Obafemi Awolowo University Teaching Hospitals Complex Ile Ife, Nigeria.

2. To determine the proportion of different skin lesions associated with diabetes mellitus

3. To assess the relationship between the glycaemic control and the skin lesions.

Materials and Methods

This study is a cross sectional prospective study conducted at the Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife. It is a tertiary care centre located in South West geopolitical zone of Nigeria. All consecutive DM patients attending the Medical outpatient department (MOPD) of Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife who meet WHO 1999 diagnostic criteria for diabetes mellitus were recruited for the study. The study was carried out between November 2009 and May 2010(six months duration)..

Approval of the ethics and research committee of the hospital was sought and obtained before the study. Informed consent of the patient for the study was also obtained.

The sample size was calculated based on documented 30% prevalence rate of cutaneous alteration among diabetics. [14] [15] [16] A total of three hundred and fifty eight(358) patients were then recruited for the study.

The patients were diagnosed to be diabetic clinically and confirmed using WHO diagnostic criteria. They include the following: Fasting plasma glucose >7.0mmol/l (126mg/dl) or random plasma glucose >11.1mmol/l (200mg/dl). One abnormal laboratory value was diagnostic in symptomatic individuals, while two values were needed in asymptomatic people. The glucose tolerance test was only required for borderline cases and for gestational diabetes.

Data were obtained from the patients using proforma that included demographic data such as age, sex, occupation and educational qualification. Date of the diagnosis of diabetes was obtained and the duration of diabetes was noted. Family history of diabetes was sought for and the type of treatment used for blood glucose control was obtained. Thorough physical examination, during which the whole skin was examined in bright light for any abnormality was carried out. Hand lens/magnifying glass was used where appropriate to make small tiny vascular changes, small scales and skin markings more obvious.

The weight of each patient was obtained using a weighing scale and the height was obtained using a stadiometer. The Body Mass Index (BMI) was calculated using weight/height [2]. BMI of 18.5- 24.9 was considered normal, <18.5 was considered underweight, 25- 29.9 was considered as overweight while >30 was considered obese.

The patients did the following investigations, full blood count, urinalysis, Fasting Blood Sugar

(FBS) + Two Hours Post Prandial (2HPP), serum electrolytes, urea and creatinine, lipid profile. Skin scrapings were done for patients with clinical diagnosis of fungal infections using sterile surgical blades, and scrapings wrapped with clean dry labeled white papers and taken to the laboratory. Mycological studies were done, and this involved placing drops of potassium hydroxide on clean flamed slides, placing small amounts of scrapped skin specimens on the slides and covering with cover slips. The samples were allowed to stand for ten minutes and thereafter examined under the microscope for fungal elements. Skin biopsy for histology was also done for confirmation when indicated.

Glycated hemoglobin level was measured for one out of every three patients (120 patients) due to economic consideration and the mean blood glucose records over 3 months period was used to assess the glycaemic control for all the patients. The mean fasting and two hours postprandial blood glucose was calculated from the average of three monthly retrospective fourth nightly or monthly documented blood glucose check. Mean FBS and 2HPP less than 7mmol/l and 10mmol/l respectively were considered as a good glycaemic control, while values greater than 7mmol/l and/or 10mmol/l respectively were considered as a poor glycaemic control. Also glycated haemoglobin percentage less than 7% was taken as good control while values greater than 7% was taken as poor glycaemic control.

Data were analyzed using a statistical computer soft ware SPSS 16.0 (Statistical Package for the Social Sciences, version 16.0). Data were represented using descriptive statistics such as tables, and charts. P value of less than 0.05 was used as level of significance.

Results

A total of three hundred and fifty five diabetic subjects were involved in the study. They comprised of one hundred and ninety two females (54.1%) and one hundred and sixty three males (45.9%). Twenty (5.7%) subjects were 40 years and below, one hundred and fifty six (43.9%) were within the 41-60 years age range while one hundred and seventy nine (50.4%) were more than 60 years old (age range: 16 - 89 years; mean = 59.76 years).

The duration of diabetes was equal to or less than 5 years in two hundred and thirty nine (67.3%) subjects, eighty one (22.8%) subjects had it for a period of between 6 - 10 years while only thirty five (9.9%) had been diabetic for more than 10 years (range: 1 - 30 years; mean = 4.91 years). Three hundred and forty seven (97.7%) subjects had type 2 diabetes and only eight (2.3%) had type 1 diabetes.

The body mass index (BMI) was above the normal range in two hundred and five (57.8%) subjects; normal in one hundred and thirty nine (39.2%) subjects and below normal in only eleven subjects **(Table 1)**.

Characters	Frequency (n)	Percent (%)
Gender		
Male	163	45.9
Female	192	54.1
Total	355	100
Age (years)		
≤ 20	2	0.6
21 – 40	18	5.1
41 – 60	156	43.9
>60	179	50.4
Total	355	100
Occupation		
Unemployed	17	4.8
Civil Servant	71	20
Farming	42	11.8
Trading	127	35.8
Pensioners	66	18.6
Artisan	24	6.8
Others (Bankers and Pastors)	8	2.3
Total	355	100
Type of Diabetes Mellitus		
Type 1	8	2.3
Type 2	347	97.7
Total	355	100
Duration of Diabetes Mellitus		
≤5	239	67.3
6 – 10	81	22.8
>10	35	9.9
Total	355	100
BMI (kg/m2)		
<18.5	11	3.1
18.5 – 24.9	139	39.2
25 – 29.9	148	41.7
≥30	57	16.1
Total	355	100

Table 1: General Characteristics of the Patients

Two hundred and fifty nine (73%) diabetics had cutaneous lesions, while ninety six (27%)

subjects had no cutaneous lesions. **Table 2** shows the prevalence of the individual lesions seen among the diabetic patients. Superficial fungal infections ranked highest and were seen in one hundred and sixty three (35.6%) diabetic patients. Pruritus was the second highest cutaneous abnormality and was present in seventy six (16.7%) subjects. The majority of the patients had generalized pruritus and they were elderly with dry skin while a few female subjects with vaginal candidiasis had localized pruritus. Diabetic dermopathy was the most common of the non-infective lesions and was seen in sixty seven (14.8%) diabetic patients in this study presented as multiple atrophic hyperpigmented shin spots.

Acanthosis nigricans was seen in twenty two (4.9%) subjects. They were seen in the axilla especially obese females. Eighteen (4.0%) subjects had diabetic thick skin, more prominent on the skin of the hand with joint contracture and obvious "prayer sign". Cutaneous bacterial infections and diabetic ulcer were each seen in sixteen (3.6%) subjects. Furuncles were the only bacterial infection documented especially in the axilla. The diabetic ulcers were on the lower limbs and the subjects affected had features suggestive of both ischaemic and neuropathic changes. Skin tags were seen in thirteen (3.0%) subjects and the majority were obese. Twelve (2.6%) diabetic subjects had tendinous xanthoma. The xanthomas were seen mainly on the finger tendons and on the wrist tendons.

Vitiligo (seen only among patients with type 2 DM rather than among patients with type 1 DM most commonly associated with it) and erysipelas-like erythema (dark brown in blacks) were each seen in ten diabetic (2.2%) subjects while sclerederma diabeticorum was observed in nine diabetic (2.0%) subjects. The subjects with vitiligo had localized, acrofacial and generalized variants. The sclerederma diabeticorum were present as induration and thickening of the skin of the upper back. Idiopathic guttate hypomelanosis was seen in seven (1.6%) subjects on the legs. Insulin lipohypertrophy was seen only among four (0.9%) diabetic subjects at the insulin injection sites on the thigh. Seborrheic dermatitis, seborrheic keratosis, and herpes zoster were seen each in two (0.45%) subjects. Seborrheic dermatitis involved the scalp and face while seborrheic keratosis were found on the face and trunk in the two cases. Herpes zoster was multi-dermatomal in both cases, and involved the thoracic dermatomes. Other cutaneous findings including Insulin lipoatrophy, diabetic rubeosis, lichen simplex chronicus, viral wart, and keloids were seen in one (0.23%) subject each. The insulin lipoatrophy was seen on the thigh, rubeosis on the cheeks bilaterally, lichen simplex chronicus above the lateral malleolus, viral wart was facial while the keloid was on the tip of the shoulder.

One hundred and twenty seven (35.8%) subjects had only one dermatological lesion each. Seventy six (21.4%) subjects had two lesions each, forty three (12.1%) subjects had three lesions, while eleven (3.1%), three (0.8%) and one (0.3%) subjects had four, five and six different types of lesions respectively.

Table 3 shows the prevalence of various superficial fungal infections seen among diabetic subjects. Tinea pedis was the most common dermatophyte infection and was seen in fifty six (15.8%) diabetic subjects with fungal infection. The majority of the patients had inter-digital tinea pedis and more than one inter-digital space was involved in most. Few subjects had plantar tinea pedis. Tinea pedis in most of the subjects have been recurrent over years, while few of the subjects had secondary bacterial infection. Tinea corporis and tinea unguium were

both present in seven (2%) and eight (2.3%) diabetic subjects respectively. Tinea unguium were seen only in the lower limbs and among subjects with tinea pedis. Cutaneous candidiasis was seen in seventy subjects of which forty (11.3%) had candidal intertrigo, thirty six (10.1%) had vaginal candidiasis and one (0.3%) had candida paronychia. The intertrigial candidiasis was seen under the breast in obese females and the groin especially among females with vaginal candidiasis and few men. Pityriasis versicolor was present in sixty seven (18.9%) diabetic subjects and were mainly truncal i.e. upper back and chest, while few patients had facial pityriasis versicolor.

Dermatological disorders	Frequency	Percent
Superficial fungal infections	163	35.4
Pruritus	76	16.7
Diabetic dermopathy	67	14.8
Acanthosis nigricans	22	4.9
Diabetic thick skin	18	4
Bacterial infection	16	3.6
Diabetic ulcer	16	3.6
Skin tag	13	3
Tendinous xanthoma	12	2.6
Vitiligo	10	2.2
Erysipelas like erythema	10	2.2
Sclerederma diabeticorum	9	2
Idiopathic gutate hypomelanosis	7	1.6
Insulin lipohypertrophy	4	0.9
Seborrheic dermatitis	2	0.45
Seborrheic keratosis	2	0.45
Herpes zoster	2	0.45
Viral wart	1	0.23
Lichen simplex chronicus	1	0.23
Keloids	1	0.23
Insulin lipoatrophy	1	0.23
Diabetic rubeosis	1	0.23

Table 2: Prevalence of dermatological disorders seen among diabetic patients (n= 355)

Infections	Frequency(n)	Percent(%)
Fungal Infections		
Tinea Infections		
Tinea corporis	7	1.50
Tinea unguium	8	1.80
Tinea pedis	56	12.30
Cutaneous candidiasis		
Candida intertrigo	40	8.80
Vaginal candidiasis	36	7.90
Candida paronychia	1	0.23
Pityriasis versicolor	67	14.80
Bacterial infections		
Furuncles	16	3.60
Viral infection		
Viral wart	1	0.23
Total	232	

Table 3: Prevalence of infections among diabetic patients (n=163)

There is a statistically significant association between blood glucose control and the presence of cutaneous lesions among the diabetics (p< 0.01) **(Table 4)** .There is also a statistically significant association between glycaemic control using glycated hemoglobin and the presence of dermatological lesions in diabetic subjects (p<0.01) **(Table 5)**.

Table 6 shows the association between infections and blood sugar control. There is a statistically significant association between infective dermatoses and blood glucose control (p<0.01), infective dermatoses being predominantly common among patients with poor blood sugar control.

Blood sugar control		Cutaneous lesions	
State	Frequency (%)	Absent (%)	Present (%)
Good	183 (51.5)	81 (44.3)	102 (55.7)
Poor	172 (48.5)	15 (8.7)	157 (91.3)
Total	355 (100%)	96 (27.0)	259 (73)
X^2 = 56.766, df = 1, P-value = 0.000			

Table 4: Pattern of glycaemic control and its association with presence of cutaneous lesions.

Glycated haemoglobin control		Dermatological lesions	
	Frequency (%)	Absent (%)	Present (%)
Good	83 (52.9)	31 (37.3)	52 (62.7)
Poor	74 (47.1)	7 (9.4)	67 (90.6)
Total	157 (100%)	38	119
X^2 = 56.766, df = 1, P-value = 0.000			

Table 5: Pattern of glycaemic control using glycated haemoglobin percentage and its association with the presence of dermatological lesions

	Blood sugar control	
Infection	Good	Poor
Present	57 (33.3)	114 (66.7)
Absent	126 (68.5)	58 (31.5)
Total	183 (51.5)	172 (48.5)
X^2 = 43.832, df = 1, P-value = 0.000		

Table 6: Association between infections and blood sugar control

Discussion

The prevalence of cutaneous lesions among diabetics in this study is 73% and is comparable to findings in earlier studies among diabetics. Mushkoor et al [18] found a prevalence of 68%, Hajieh et al [19] and Khurshid et al [20] established a prevalence of 92% and 76.6% respectively in their research work on diabetics while Onunu et al [17] in their work in Benin, Nigeria were able to document a prevalence of 63.2% among diabetics. These observations across divergent populations and races across the globe buttressed the assertion that dermatological disorders are common among diabetic subjects.

Infection is the most common of the dermatoses seen among the diabetic subjects in this study. The overall prevalence of infection was 39.2%. Superficial fungal infections accounted for 35.4% while bacterial infection accounted for 3.6%. This finding is similar to that of Onunu et al [17] where infection had the highest prevalence, accounting for 38.8% of dermatoses seen in a diabetic population. Nawaf Al-mutari et al [21] found infection in 67.2% of their study population, while Mashkoor et al [18] found infection in 37.5% of their patients. In all these studies, the prevalence of fungal infection was consistently higher than bacterial infection. Poor glycaemic control was responsible for the significantly high prevalence of infection in this

study (p<0.01). Infections thrive in a setting of poor glycaemic control and opportunistic organism, like candida albicans, causes active infection in an environment with elevated blood glucose. The low prevalence of bacterial infection in this study as compared to fungal infection could be because bacterial infections respond readily to short course of over-the-counter antibiotics which many patients still engross in while fungal infection will either persist or re-occur following short course of such over-the counter antifungals.

Tinea pedis was the most common of dermatophyte infections in this study with a prevalence of 12.3%. This is consistent with the study by Al-mutari et al [21] where it was also the commonest of dematophytes with a prevalence of 21%. Diabetics are at an increased risk of T. pedis because of the high prevalence of dry skin in them which predisposes to inter-digital or web space cracking which in the presence of moisture from retained sweat and suboptimal glycaemic control perpetuate the infection.

Herpes zoster was documented in two elderly diabetic patients with chronic hyperglycaemia. herpes zoster though not pathognomonic of DM can occur especially among elderly diabetic where old age and chronic hyperglycaemia can act as cruel synergy in causing immune suppression leading to activation of herpes zoster.

Pruritus had been observed to occur in diabetic patients with a prevalence varying widely from a level as low as 2.7% to a level as high as 49 % respectively. [17], [18], [20], [26] In this study, pruritus was seen in 16.7% of subjects. This high prevalence of pruritus could be due to dry skin which is common in diabetes and can predispose to generalized pruritus and also possibly because of high prevalence of fungal infection in diabetes which can predispose to localized itching. Furthermore, over half of the subjects in this study were above 60 years of age, and dry skin is more common in people above 60 years of age and this can predispose to itching.[27]

Acanthosis nigricans was seen in 4.9% of the subjects in this study. In other studies, it was seen in 13% of African Americans and 6% of Hispanics. [22] Acanthosis nigricans could be due to insulin resistance, hyperinsulinaemia, stimulation of fibroblast synthesis through insulin growth factor 1 and obesity which are all predominant in type 2 DM.

Diabetic thick skin and sclerederma diabeticorum were seen in 4.0% and 2.0% of patients respectively in this study. Rosenbloom et al [23] reported thick skin in 33.3% of type 1 diabetics with joint limitation. Sclerederma diabeticorum was however reported in 2.5% of patients with type 2 DM [24] a prevalence similar to that in this study. The reason for lower prevalence of diabetic thick skin in this study could be attributed to the fact that 98% of cases examined had type 2 DM whereas Rosenbloom studied subjects with type 1 DM only with possible high prevalence of thick skin compared to type 2 DM. [23]

Neuropathy, peripheral vascular disease, and microangiopathy play important role in the initiation of diabetic ulcer, while poor glycaemic control is important in the non-healing nature of the ulcers.

Skin tags had a prevalence of 3.0% in this study. The prevalence vary widely in other previous

studies, 33.82%,10.4% and 3.7% respectively by Maskoor et al [18], Nawaf Al-mutari et al [21], and Khurshid Ahmed et al. [20] The variation could be due to differences in the prevalence of obesity in populations studied. Skin tags have close association with obesity which is common in type 2 DM.

Tendinous xanthoma was seen in 2.6% of subjects in this study. The prevalence in previous studies were 6.6% and 2.6% by Nawaf Al-mutari et al [21] and Khurshid et al. [20] Diabetes mellitus is an important cause of acquired dyslipidaemia especially hypertriglyceridaemia which predisposes to xanthomas. [24]

The prevalence of vitiligo was 2.2% in this study and is similar to a prevalence of 2.8% reported by Nawaf Al-mutari et al. [21] Dawber reported a prevalence of 4.8% among 520 diabetic patients.[25] Though the prevalence is low, it is possible that vitiligo occurred in some diabetic patients with shared autoimmune etiology. Also majority of the subjects in this study suffer from type 2 DM which is genetic and life style related rather than autoimmune that is commoner in type 1 DM.

Idiopathic guttate hypomelanosis was seen in 1.6% of the subject examined. It was seen among middle aged and elderly subjects. This finding may be incidental, though further study involving screening all patients with idiopathic guttate hypomelanosis for DM may need to be undertaken to exclude or establish a relationship between the two conditions.

The prevalence of insulin lipohypertrophy and Insulin lipoatrophy in this study were 0.9% and 0.23% respectively. This is similar to 1.6 and 0.4% reported by Onunu et al. [17] The reason for the low prevalence of these insulin injection associated reactions is likely due to wide use of highly purified insulin with very low tendency for adverse reactions. Furthermore, majority of the subjects in this study had type 2 DM and were on oral hypoglycaemic agents.

Diabetic rubeosis was seen only in one patient (0.3%).The reported prevalence in the literature was 59%. [26] The reason for rarity of rubeosis in this study could be due to the dark skin type of the population studied which made it very difficult for facial erythema to be appreciated. It was only evident in one patient with very fair skin color.

Glycaemic control was detected by the average of monthly blood glucose levels for three months and glycated hemoglobin which were similar and are both important determinant of cutaneous lesion especially the infective lesions which were due to poor glycaemic control with a p value of <0.01. This is similar to the finding by Khurshid et al [20] where poor glycaemic control was the most important determinant of presence of cutaneous lesions among diabetic subjects. Poor glycaemic control impairs immune response to infection including leukocytosis, chemotaxis and phagocytosis, and this may be the reason for the high prevalence of infective lesions among diabetics.[28]

Conclusion

The prevalence of dermatological disorders among the diabetics in this study is 73%. The commonest lesion noticed being infectious dermatoses especially fungal infections. The high

prevalence of these fungal infections and their persistence and recurrence following treatment can be a pointer to DM.

Since patients with diabetes tend to have multiple lesions as documented in this study, the presence of multiple dermatological lesions in an individual especially the infective ones could be a pointer to suspicion and diagnosis of diabetes.

Poor glycaemic control is an important determinant of presence of cutaneous lesions and most of these lesions especially multiple infective lesions may be pointers to suspicion and diagnosis of diabetes.

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