PATTERN OF DERMATOLOGICAL DISORDERS AMONG DIABETIC PATIENTS IN OBAFEMI AWOLOWO UNIVERSITY TEACHING HOSPITAL COMPLEX, ILE-IFE, NIGERIA.

A DISSERTATION SUBMITTED TO THE NATIONAL POSTGRADUATE MEDICAL COLLEGE OF NIGERIA IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE AWARD OF THE FELLOWSHIP OF THE COLLEGE IN THE FACULTY OF INTERNAL MEDICINE

SUBSPECIALITY: DERMATOLOGY

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DECLARATION

I hereby declare that this work is original unless otherwise acknowledged. The work has not been presented to any other college for a fellowship nor has it been submitted elsewhere for publication.

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CERTIFICATION

The study reported in this dissertation was done by the candidate under our supervision. We have also supervised the writing of the dissertation.

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TABLE OF CONTENTS

Title page i
Declaration ii
Certification iii
Attestation iv
Table of contents v
List of tables vii
List of figures ix
Keys to abbreviation x
Dedication xi
Acknowledgment xii
Summary xiii

CHAPTER ONE
Introduction 1

CHAPTER TWO
Objectives 6

CHAPTER THREE
Justification of the Study 7

CHAPTER FOUR
Literature Review 8

CHAPTER FIVE
Methodology 46
# CHAPTER SIX

Results 53

# CHAPTER SEVEN

Discussion 101
Conclusion 112
Recommendations 113
References 114
Appendix 1 Proforma 138
Appendix ii Informed Consent Sheet 142
Appendix iii Ethical Clearance 143
LIST OF TABLE

Table 1: General Characteristic of the Patients 54
Table 2: Prevalence of dermatological disorders seen among diabetic patients. 59
Table 3: Prevalence of infections among diabetic patients 60
Table 4: Prevalence of dermatophyte species in diabetic patients with Tinea pedis 61
Table 5: Pattern of glycaemic control and its association with presence of cutaneous lesions. 64
Table 6: Pattern of glycaemic control using glycated haemoglobin percentage and its association with the presence of dermatological lesions 65
Table 7: Association between infections and blood sugar control 66
Table 8: Association between gender and presence of dermatological lesions 70
Table 9: Association between age and presence of dermatological Lesions 71
Table 10: Association between socioeconomic class and presence of dermatological lesions 72
Table 11: Association between type of DM and presence of dermatological lesions 73
Table 12: Association between duration of diabetes mellitus and presence of cutaneous lesions 74
Table 13: Association between Type of treatment and lesions 75
Table 14: Association between BMI and lesions 76
Table 15: Prevalence of other complications of diabetes 79
Table 16: Association between Neuropathy and the presence of cutaneous lesions. 80
Table 17: Association between Hypertension and the presence of cutaneous lesions. 81
LIST OF FIGURES

Figure 1: Interdigital Tinea Pedis 82
Figure 2: Planter Tinea Pedis 83
Figure 3: Furuncles 84
Figure 4: Vaginal Candidiasis 85
Figure 5: Diabetic Dermopathy 86
Figure 6: Acanthosis Nigrican 87
Figure 7: Tendinous Xanthoma 88
Figure 8: Vitiligo 89
Figure 9: Skin Tag 90
Figure 10: Scleredema Diabeticorum 91
Figure 11: Diabetic Thick Skin with Prayer Sign 92
KEY OF ABBREVIATIONS

DM – Diabetes Mellitus
T2DM – Type 2 Diabetes mellitus
CAD – Coronary Artery Disease
CVA – Cerebrovascular Accident
PVD – Peripheral Vascular Disease
NLD – Necrobiosis Lipoidica Diabeticorum
GDM – Gestational Diabetes Mellitus
IDDM – Insulin Dependent Diabetes mellitus
NIDDM – Non- Insulin Dependent Diabetes mellitus
ADA - American Diabetes Association
NEG – Non – enzymatic Glycosylation
LJM – Limited Joint Mobility
WHO – World Health Organization
FBS – Fasting Blood Sugar
2HPP – 2 Hours Post Prandial
MOPD – Medical Out- patient Department
PKC – Protein Kinase C
DNA – Deoxy ribonucleic acid.
IGF-1 – Insulin growth factor – 1
MRNA – Messenger Ribonucleic acid.
GA – Granuloma Annulare.
PUVA – Psoralen Ultraviolet A.
EBV – Ebstein bar virus.
TB – Tuberculosis.
AIDS – Acquired Immunodeficiency Syndrome.
DEDICATION

This dissertation is dedicated to God Almighty, the Ancient of Days who made all things possible.
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SUMMARY

The study was carried out to determine the prevalence and pattern of dermatological disorders among diabetic patients in Obafemi Awolowo University Teaching Hospital Complex Ile-Ife, and to assess the relationship between duration of diabetes, glycaemic control and the dermatological disorders.

A purpose designed questionnaire was used to obtain the following information from the subjects; age, gender, occupation, educational qualification, duration of diabetes, family history of diabetes mellitus, type of treatment received. History of present complications of diabetes was sought and the subjects were examined from head to feet for presence of skin lesions. The lesions seen were documented and specimen taken and sent when necessary to the laboratory for microscopy and culture. Skin biopsy was also taken for confirmation of diagnosis when necessary.

The weight and height of the subjects were measured and used to calculate the body mass index (BMI). Average of three monthly fasting blood glucose and two hours post prandial glucose was calculated for all subjects to assess blood glucose control. Glycated haemoglobin was measured for one hundred and fifty seven subjects and was also used to assess glycaemic control.

A total of three hundred and fifty five subjects were involved in this study. One hundred and ninety two (54.1%) subjects were females and one hundred and sixty three (45.9%) were males. Age range of the subjects was 16 – 89 years with mean of 59.76 years. Duration of diabetes ranged from 1 – 30 years with mean of 4.91 years.
The prevalence of dermatological disorders found in this study was 73%. Infectious dermatoses (39.2%) especially fungal infections (35.4%) constituted the bulk of the dermatological disorders seen in this study. Other disorders seen included pruritus (16.7%), diabetic dermopathy (14.8%), acanthosis nigricans (4.9%), diabetic thick skin (4.0%), bacterial infection (3.6%), diabetic ulcer (3.6%), skin tags (3.0%), tendinous xanthoma (2.6%), vitiligo (2.2%), erysipelas like erythema (2.2%), sclerederma diabeticorum (2.2%), idiopathic guttate hypomelanosis (1.6%) insulin lipohypertrophy (0.9%), seborrheic dermatitis (0.45%), herpes zoster (0.45%), viral wart (0.23%), lichen simplex chronicus (0.23%), keloids (0.23%), insulin lipoatrophy (0.23%), and diabetic rubeosis (0.23%).

Rare cutaneous disorders linked to diabetes such as granuloma annulare, acquired perforating disorder, necrobiosis lipoidica and bullosis diabeticorum were not seen in this study.

Poor glycaemic control was a major determinant of presence of dermatological disorders among the subjects in this study. Disorders were seen in higher frequency among subjects with poor glycaemic control (p < 0.01). This is especially so for infective dermatological disorders because poor glycaemic control alters immune status and predisposes patients to infections. Dermatological disorders were also seen more among subjects who had been diabetic for less than or equal to five years (p=0.042). This may be incidental because majority of the subjects in the study (67.3%) have been diabetic for just less than 5 years. Factors such as age, gender, occupation, type of diabetes did not contribute to the presence of dermatological disorders among diabetic population (p>0.05).
Other complications of diabetes such as neuropathy and hypertension, were seen in higher frequency among diabetic patients with dermatological lesions, though they did not show any significant statistical association except hypertension \( (P = 0.026) \).

This study therefore showed high prevalence of dermatological disorders in patients with diabetes mellitus and poor (suboptimal) glycaemic control was the major contribution to the presence of these disorders.
CHAPTER ONE

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 afflicts approximately 60 million people globally.² However, between 1958 and 1993 the number of individuals diagnosed with diabetes mellitus increased five fold.³ It has been estimated by the World Health Organization (WHO) that the incidence will rise to 300 million by the year 2025.

Over the past century, diabetes mellitus (DM) has been considered as a rare medical condition in Africans as illustrated by the famous statement of Dr. Cook who wrote that “Diabetes is very uncommon but very fatal” in his 1901 notes on the disease met in Africans.⁴ However, epidemiological studies carried out in the last decade of the 20th century have provided evidence of a different picture. There is a global trend towards an increase in the incidence and prevalence of diabetes in African population.⁵ Indeed, Africa is experiencing one of the most rapid demographic and epidemiological transitions of the world history.⁶
The rise in prevalence of diabetes mellitus and other non-communicable diseases in Africa is due to increasing aging of the population and westernization of life style. Type 2 diabetes (T2DM) is the predominant form, yet, a classification problem persists for a proportion of patients. According to an Ibadan study, the prevalence of diabetes mellitus in Nigeria was put at 0.8% and impaired glucose tolerance at 2.2% with no sex difference. Erasmus et al in 1989 gave the prevalence of diabetes mellitus to be 1.4% among a mixed urban/rural population, whereas a study by Ohwovoriole et al in 1988 in an urban community gave a prevalence of 1.7%. A report from the national expert committee on non-communicable diseases in Nigeria, put the prevalence of diabetes among males and females at 2.7 and 3.0% respectively with an average of 2.8% in both sexes.

Better understanding of the pathophysiology of T2DM has led to improved therapeutic modalities. However, the incidence/prevalence of the vascular complications remains high and has emerged as a leading cause of the increased morbidity and mortality.

Disease of blood vessels as a consequence of diabetic angiopathy affects both the large vessels – (macroangiopathy) and
small capillaries (microangiopathy). Affectation of the small vessels cause retinopathy, neuropathy, nephropathy and dermopathy.\textsuperscript{14}

Interest in the skin manifestation of diabetic microangiopathy started in 1964 when Bauer et al\textsuperscript{15} demonstrated periodic acid-schiff positive capillary basement membrane thickening (CBMT) in necrobiosis lipoidica diabeticorum (NLD) which was similar to changes seen in diabetic microangiopathy in dermopathic lesion by Binkley\textsuperscript{16} and in granuloma annulare. Other workers\textsuperscript{17} have also suggested that the underlying pathology of bullosis diabeticorum and rubeosis may be microangiopathy.\textsuperscript{18,19}

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 the underlying disease.\textsuperscript{20} 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.\textsuperscript{21}
The complications of diabetes in Nigeria have been studied by many authors.22-26 These studies indicate that diabetic complications are important cause of morbidity and mortality among diabetics, however majority of these studies did not look at the cutaneous problems.

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 chronic nature of the disease.27-29 In 1995, Onunu et al.30 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 antidiabetic treatment.
CHAPTER TWO

OBJECTIVES

1. To determine the prevalence and pattern of skin lesions among diabetic patients in OAUTHC
2. To determine the proportion of different type of skin lesions associated with diabetes mellitus
3. To determine the relationship between duration of diabetes and these skin lesions
4. To determine the relationship between glycaemic control and skin lesions.
CHAPTER THREE

JUSTIFICATION OF THE STUDY

Studies of the pattern of dermatological disorders among diabetics in Nigeria are limited. The outcome of this study will be compared with previous studies and help draw attention to the magnitude of the problem among diabetics in Nigeria.

The study may also help predict the relationship of skin lesions with glycaemic control and other complications of diabetes mellitus.
CHAPTER FOUR

LITERATURE REVIEW

Diabetes mellitus is a heterogenous group of disorder characterized by elevated serum glucose levels resulting from defects in either the insulin production or insulin action or a combination of both. Complications include retinopathy, nephropathy and neuropathy. The two main types of diabetes are type I diabetes mellitus which is characterized by the destruction of insulin producing beta cells of the pancreas thereby creating the absolute need for exogenous insulin, and type 2 diabetes mellitus which is associated with old age, obesity, physical inactivity and family history. However Type 2 diabetes mellitus is increasingly being diagnosed in children and adolescents as well and is linked to childhood obesity and diet.\textsuperscript{15}

Nearly one third of diabetic patients have some type of dermatological manifestations.\textsuperscript{27} With time the skin of all diabetic patients is affected in one form or another hence understanding the cutaneous signs of diabetes is extremely valuable to the clinician. For example diabetic bullae, diabetic dermopathy, necrobiosis lipiodica diabeticorum and the scleroderma like syndrome of waxy
skin with limited joint mobility can alert the physician to the diagnosis of diabetes.16-18

4.2 Classification of Diabetes Mellitus

Diabetes mellitus is classified on the basis of the pathogenic process that leads to hyperglycaemia, as opposed to earlier criteria such as age of onset or type of therapy. This classification is as listed below:

Aetio logical classification of diabetes mellitus.31

i. Type I diabetes
   a. Immune Mediated
   b. Idiopathic
   
   ii. Type 2 diabetes
   
   iii. Other specific types of diabetes
      a. Genetic defect of B-cell function
      b. Genetic defect of insulin action
      c. Diseases of exocrine pancreas
      d. Endocrinopathies
      e. Drugs or chemical induced
      f. Infections
      g. Uncommon form of immune mediated diabetes
h. Other genetic syndromes associated with diabetes mellitus

iv. Gestational diabetes mellitus (GDM)

Two features of the current classification of diabetes mellitus diverge from previous classification. Firstly, the terms insulin dependent diabetes mellitus (IDDM) and non-insulin dependent diabetes mellitus (NIDDM) are obsolete. Secondly, since many people with type 2 DM eventually require insulin treatment for control of glycaemia, the use of the term NIDDM could generate considerable confusion. Furthermore, type I DM most commonly occur before age 30, however, an autoimmune beta cell destruction process for instance, can develop at any age.

4.3 DIAGNOSIS

Recently, there has been major growth in the knowledge of the aetiology and pathogenesis of different types of diabetes and about the predictive value of different blood glucose levels for the development of complications. Both the American Diabetes Association (ADA) and the World Health Organization (WHO) have re-examined, redefined and updated the classification of and the criteria for diabetes, which have been unchanged since 1985.
The recent criteria are given below:

**WHO diagnostic criteria 1999:**

- Fasting plasma glucose > 7.0 mmol/L (126 mg/dl)
- Random plasma glucose > 11.1 mmol/L (200 mg/dl)
- One abnormal laboratory value is diagnostic in symptomatic individuals
- Two values are needed in asymptomatic people
- The glucose tolerance test is only required for borderline cases and for diagnosis of gestational diabetes.

**The glucose tolerance test – WHO criteria**

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Impaired</th>
<th>Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting</td>
<td>&lt;7 mmol/l</td>
<td>6.1-6.9 mmol/l</td>
<td>&gt;7 mmol/l</td>
</tr>
<tr>
<td>2hrs after glucose</td>
<td>&lt;7.8 mmol/l</td>
<td>between 7.8-11.0 mmol/l</td>
<td>11.1 mmol/l or more</td>
</tr>
</tbody>
</table>

- For the glucose tolerance test, 75g of anhydrous glucose in 300mls of water is taken.
- There is no such thing as mild diabetes, all patients who meet the criteria for diabetes are liable to disabling long term complications.
4.4 PATHOPHYSIOLOGY OF CUTANEOUS MANIFESTATIONS OF DIABETES MELLITUS

Nearly all patients with diabetes mellitus have cutaneous manifestations. Although the mechanisms for many DM-associated skin conditions remain unknown, the pathogenesis of others is linked to hyperglycaemia and insulin dysfunction, either directly, or through damage to the vascular, neurologic, or immune systems.

Six prominent theories, which are not mutually exclusive, have been proposed to explain how hyperglycaemia might lead to the skin complications of diabetes mellitus:

1. **Non-enzymatic glycosylation (NEG).**

   Non-enzymatic glycosylation of various structural and regulatory proteins, including collagens occur in a state of hyperglycaemia. NEG occur with aging but is greatly accelerated in diabetes mellitus. NEG leads to the formation of advanced glycosylation end products (AGES) that are responsible for decreases in both acid solubility and enzyme digestion of cutaneous collagens. Disorders such as diabetic thick skin and limited joint mobility (LJM) are thought to result directly from accumulation of AGES.
Studies show that the degree of cutaneous AGES correlates strongly with retinopathy, nephropathy and other microvascular complications of DM\textsuperscript{35}.

2. **Macro and microangiopathy**

Macro and microangiopathy contribute significantly to the cutaneous complications of DM. Microvascular abnormalities include leakiness or vessel wall permeability, decrease response of vessels to sympathetic innervations, and less ability to respond to thermal and hypoxaemic stress.\textsuperscript{36} In combination with the arteriosclerosis of macroangiopathy, these microvascular abnormalities contribute to the development of diabetic ulcers.

Aldose reductase polymorphisms have been described in relation to microvascular disease.\textsuperscript{37} Aldose reductase uses nicotinamide adenine dinucleotide phosphate (NADPH) to reduce glucose to sorbitol. The accumulation of sorbitol leads to a decrease in NADPH, myo-inositol and Na+/K+-dependent adenosine triphosphate and glutathione.\textsuperscript{38} These biochemical changes cause endothelial injury.\textsuperscript{39,40}

The metabolic derangements of hyperglycaemia results in reduced antioxidant defences. Hyperglycaemia generates
reactive oxygen species, which leads to glucose auto-oxidation.\textsuperscript{41} Such oxidant stress may disrupt endothelial function by inactivating nitric oxide.\textsuperscript{42,43}

Activation of protein kinase C (PKC) is a likely common pathway for endothelial abnormalities in diabetes. Phospholipases may be upregulated by reversible oxygen intermediates and advanced glycated end products, and this may increase diacylglycerol levels which activate PKC.\textsuperscript{44} Activation of PKC may lead to induction of several growth factors including transforming growth factor-$B$ and vascular endothelial growth factor as well as nuclear transcription factor.

3. **Loss of cutaneous sensory innervation**

Loss of cutaneous sensory innervation occurs in diabetes mellitus, predisposing to infection and injury. The loss of neuroinflammatory cell signaling plays a causal role in non-healing lower extremities ulcer.\textsuperscript{45}

4. **Immunoregulatory derangement**

Hyperglycaemia and ketoacidosis diminish chemotaxis, phagocytosis, and bactericidal ability of white blood cells.\textsuperscript{36} Certain infection such as streptococcal pyoderma,
candidiasis, and the more devastating mucormycosis and necrotizing fascitis, do appear to be associated with poorly controlled diabetes mellitus.\textsuperscript{46}

5. **Dysregulation of lipid metabolism**

Dysregulation of lipid metabolism occurs with DM-associated insulin deficiency. The activity of lipoprotein lipase is directly dependent on insulin,\textsuperscript{47} making insulin central to the processing of triglyceride rich chylomicrons and very-low-density lipoprotein (VLDL). In insulin deficient diabetics, defective lipid processing may lead to massive hypertriglyceridaemia, manifesting in the skin as eruptive xanthomas.

6. **Altered Gene Expression**

Hyperglycaemia was found to increase synthesis of matrix molecules, fibronectin, laminin and type IV collagen in endothelial cells cultured with high glucose concentration, and this was found to be due to altered gene expression.\textsuperscript{48} These changes remained despite normalization of blood glucose, suggesting a permanent DNA level alteration.

The mechanisms by which hyperglycaemia leads to increased gene expression is not clear,\textsuperscript{49} but it is thought that
glucotoxicity from the activation of protein kinase C, and the cross-linking of DNA with nucleoprotein among others, induce DNA damage and altered transcription which specifically activates the expression of co-ordinated set of growth-associated and angiogenesis-associated genes.\textsuperscript{50,51}

4.5 CUTANEOUS MANIFESTATIONS OF DIABETES MELLITUS

At least 30% of diabetic patients have skin alterations which are related to diabetes mellitus, whereas some authors believe that the percentage may climb to 100% primarily due to the chronic nature of the disease.\textsuperscript{27-29} These skin changes may be due to microangiopathy, arteriosclerosis, infection, direct metabolic disturbances and /or sequelae of chronic therapy.\textsuperscript{52} The various categories of cutaneous lesion include the following:

1. **Cutaneous lesions due to vascular abnormalities**
   - Diabetic dermopathy
   - Diabetic rubeosis
   - Diabetic ulcers
   - Erysipelas – like erythema
2. **Cutaneous infections in DM**

- **Bacteria Infections**
  - Group A and B streptococcal infection
  - Necrotizing fascitis
  - Malignant otitis media

- **Mycotic Infections**
  - Hands and feet candidiasis
  - Rhinocerebral mucormycosis
  - Onychomycosis

3. **Various skin disorders associated with diabetes mellitus**

- Acanthosis nigricans
- Diabetic thick skin
- Eruptive xanthoma
- Necrobiosis lipoidica
- Granuloma annulare
- Scleredema diabeticorum
- Acquired perforating disorder
- Bullosis diabeticorum
- Pruritus
- Vitiligo
• Yellow skin
• Skin tags

4. **Skin disorder associated with insulin therapy**

• Local insulin reaction

**DIABETIC DERMOPATHY**

This is the most common dermatosis associated with diabetic mellitus, microangiopathy and possibly neuropathy, are involved. Diabetic dermopathy is pathognomonic for diabetes mellitus, affecting 7-70% of all diabetic patients. It was first characterized and presented as cutaneous marker for DM by Melin in 1964.

Binkey coined the name to correlate the pathologic changes with those of retinopathy, nephropathy and neuropathy. Lesion occurs predominantly on the shin (Shin spots), forearm, thighs and over bony prominences. The lesion is an oval, dull red papule which is between 0.5-1cm in diameter. It evolves slowly, producing superficial scale, and leaves atrophic brown scar. The colour is due to haemosiderin in histocytes near the vessels.

The lesions are usually bilateral but not symmetrically distributed. They are asymptomatic and often overlooked.
In known diabetics, it has been advocated that the occurrence of dermopathic lesions should initiate an investigation for diabetic microangiopathy and neuropathy.\textsuperscript{59} The frequency of diabetic dermopathy increases with age and duration of diabetes. It is seen most typically in elderly patients and in young patients with type 1 diabetes mellitus of long duration.\textsuperscript{60} This is because microangiopathy which is a risk factor for and accompaniment of dermopathy tends to occur with increased duration of diabetes. An association exist between diabetic dermopathy and the more serious complications of DM. In a study of 173 patients with DM, the incidence of shin spots was significantly increased in patients with retinopathy, nephropathy and neuropathy\textsuperscript{61}. Nawaf AL-Mutari et al\textsuperscript{62} found diabetic dermopathy in 5.7\% of 106 diabetic patients studied, Mashkoor et al\textsuperscript{63} found similar lesion in 8.08\% of 200 DM patients, Yasmeen J Bhat et al\textsuperscript{64} in 17 (11.3\%) of 150 patients, Hajieh Shhbazian et al\textsuperscript{65} in 22\% of their patients with no significance correlation between the type of diabetes and HbA1C, and skin manifestation. However 40\% of diabetic patients in an Israeli hospital had diabetic dermopathy.\textsuperscript{66}

Histologic characteristics of acute lesions are edema of the epidermis and papillary dermis, extravasated erythrocytes and a
mild lymphohistiocytic infiltrate. Older lesions have thick walled capillaries in the upper dermis, occasional extravasated erythrocytes and a positive stain for iron. Electron microscopy study however demonstrated the presence of thickened basal lamina only in some patients. No treatment is necessary for the individual atrophic tibial lesions as they are asymptomatic and are not directly associated with an increase in morbidity.

**DIABETIC RUBEOSIS**

This is due to facial involvement of microangiopathy. There is rosy reddening of the face, and sometimes of the hands and feet. Facial erythema in diabetic patients was first described in the early 1900s. Hyperglycaemia predisposes to sluggish microcirculation and affected individuals develop functional microangiopathy which is clinically evident by venous dilatation. Microangiopathy may be involved in damage to the capillaries, similar to the changes of rosacea, in which it has been shown that capillary damage causes abnormalities of connective tissue resulting in venous dilatation. Hypertension, which often coexists with diabetes is also common in these patients and may exacerbate the capillary damage. The intensity of red colouration depends on the degree of engorgement of the superficial venous plexus. It may be evident in newly
diagnosed diabetics and, more importantly, the vascular engorgement may return to normal when blood sugar is controlled.

In a prospective Israeli study of 150 medical hospital admissions comparing facial redness (none, slight red, or markedly red) with diabetic parameters (persisting fasting hyperglycaemia or a diabetic glucose tolerance curve), of 61 patients with diabetes, thirty six (59%) had marked red face. Because of normal variation in complexion, this sign is difficult to use as a marker of microangiopathy especially in Nigerians.

Yasmeen J Bhat et al demonstrated rubeosis in 2 (1.3%) of 150 diabetic patients they studied, Hajieh Shahbazian et al in 2% of 100 DM patients, Mashkoor Ahmed Wani et al in 6 (4.41%) of 200 diabetic patients, whereas Nawaf Al-Mutari et al demonstrated it in 11 (10.4%) of 106 diabetic patients they examined.

**DIABETIC ULCERS**

Of all the cutaneous conditions associated with diabetes, skin ulceration has by far the greatest clinical impact. Approximately 15% of persons with diabetes will have a foot ulcer in their lifetime, and diabetic foot ulcers and gangrene are the leading causes of hospitalization in patients with diabetes mellitus. Approximately
85% of all diabetes-related lower extremity amputations are preceded by foot ulcers.\textsuperscript{74}

The aetiology of diabetic foot ulcers is typically multifactorial. Many of the risk factors for foot ulcer are also predisposing factors for amputation, and often occur in patients with peripheral vascular disease and infection. The following factors are important;

1. **PHYSICAL FACTORS.** Altered foot biomechanics, limited joint mobility, and bony deformities have been associated with an increased risk of ulceration and amputation. Abnormalities in foot biomechanics result in a dysfunctional gait, which leads to more damaging structural changes in the foot. Abnormal pressure points result in increased friction. Bony deformities of the metatarsal heads and forefoot result in areas of increased focal pressure which are susceptible to breakdown. These areas are susceptible to infection once the skin surface is broken.

2. **NEUROPATHY.** Neuropathy is a major contributing risk factor to foot ulcers. It causes loss of pain sensation, and as a result repeated trauma and increased shear forces affect the skin, without any aversive response.\textsuperscript{75} Skin breakdown goes unnoticed and may worsen.
3. VASCULAR ISCHAEMIA. Local ischaemia as a result of both large and small vessel disease is a major cause of skin ulceration. Wound healing requires an increase in skin blood flow, whereas peripheral vascular disease limits blood flow to the skin and hence impairs wound healing. It is well established that microangiopathy impairs skin perfusion more in diabetics with peripheral vascular disease than in non-diabetics with the same degree of large vessel impairment. Diabetic neuropathy also contributes to abnormal vasodilatation, further impairing microvascular blood flow.

Diminished perfusion as a result of diabetic microangiopathy decreases tissue resistance, leads to rapid tissue death, and impedes wound healing by reducing the supply of oxygen, nutrients, and mediators of repair process. In the diabetic foot, insufficient capillary perfusion and inability of the capillaries to vasodilate in response to injury lead to a functional ischaemia of the skin.

Basement membrane thickening does not cause an obstruction of flow, but limits the ability of white blood cells to migrate to a site of injury. A reduction in the number of white blood cell can lead to infection and ulceration. Furthermore, in the
healing wound, migration of blood-borne monocytes to the site contributes to vigorous production of a host of families of growth factors.\textsuperscript{80} Platelet-derived growth factors, vascular endothelial growth factor, fibroblast growth factors, and epidermal growth factor are all strongly expressed. Decreased blood flow limits the influx of these factors.

Microangiopathy also impairs tissue oxygenation. Hyperbaric oxygen therapy has been shown to be successful in correcting reduced oxygen tension in ischaemic tissue.\textsuperscript{81} Oxygen therapy induces angiogenesis in wounds, thereby augmenting the microvascular system which has been impaired by diabetic microangiopathy.\textsuperscript{82-83} Hyperbaric oxygen treatment is effective in salvaging very devitalized tissues, including diabetic foot ulcers.\textsuperscript{84}

4. **VENOUS STASIS.** Diabetic patients are subject to venous stasis ulcers.\textsuperscript{85} Many diabetics are obese, and visceral obesity leads to increased pressure in the inferior vena cava. This in turn increases lower extremity venous pressure.\textsuperscript{86} Therefore varicose veins are more common in obese patients, and skin breakdown occurs in areas of increased venous pressure. The long term healing prognosis for leg ulcers is poor and worse for patients with venous ulcers.
**ERYSIPELAS LIKE ERYTHEMA**

Another reported phenomenon of microcirculatory compromise in diabetic patients is the development of well demarcated erythema of the lower leg or dorsum of the foot that correlates with radiological evidence of underlying bone destruction, and incipient gangrene.\(^{87,88}\) It is seen mostly in elderly patients with an average duration of diabetes mellitus of 5 years. Cardiac decompensation may be involved. The condition was first mistaken for erysipelas (hence the name erysipelas-like erythema), but there was no associated pyrexia, elevated erythrocyte sedimentation rate or leukocytosis. The erythema would seem to be functional microangiopathy localized to an area of microcirculation compromise.

**CUTANEOUS INFECTIONS**

A lot of work have been done on the pathogenesis of immune dysfunction in DM. Some studies could not detect any defect at the cellular level\(^{89}\) however, other studies show that leukocyte chemotaxis, adherence, and phagocytosis are impaired in patients with DM, especially during hyperglycaemia and diabetic acidosis.\(^{90}\)
Some other studies also show decreased cutaneous T-cell function and response to antigen challenge.\textsuperscript{46}

In the pre-insulin era, the prevalence of common pyodermas such as furunculosis, carbunculosis, and erysipelas was much higher for diabetics than their non-diabetic counterparts.\textsuperscript{91} Today these infections do not appear to be higher in prevalence among diabetics.\textsuperscript{92} However, there are several infections which characteristically occur in persons with DM, and some of them could be life threatening.

Patients with DM are at higher risk of contracting certain bacterial infections e.g. Group A and B streptococcal infection, necrotizing fasciitis, and malignant otitis media. In a study of 424 non pregnant adults with invasive group B streptococcal infection, 30\% of cases occurred in patients with DM.\textsuperscript{93} In young adults, the presence of DM increases the risk of group B streptococcal infection 30-fold and invasive group A streptococcal disease 3.7 fold.\textsuperscript{93}

Malignant external otitis, an uncommon but serious infection of the external ear canal by pseudomonas, characteristically presents as purulent discharge in an elderly diabetic patients.\textsuperscript{94}
The infection begins as cellulitis of the ear canal, but natural cleavage planes allow progression through osseous cartilagenous junction. Approximately 70-94% of patients with malignant external otitis have DM.\textsuperscript{95} Mortality is 20-40% despite appropriate antibiotic therapy.\textsuperscript{46}

Necrotising fasciitis is a life threatening bacterial infection of the soft tissues with spread along fascial planes. The perineum, trunk, abdomen, and upper extremities are most commonly involved and the mortality rate could be as high as 40%.\textsuperscript{46}

Yeast infections are common in diabetic patients, involvement of the glans penis and vulva appear common in type II diabetes. Vaginal candidiasis is almost universal among women with long term diabetes, and yeast infections may even be the presenting manifestation of diabetes.\textsuperscript{96} It is the common cause of pruritus vulvae during glycosuria. Presenting sign include vulva erythema, accompanying by fissuring and whitish vaginal discharge. Angular stomatitis occurs especially in children and occasionally in adult due to increased saliva glucose concentration.\textsuperscript{97}

The prevalence of candida of the hands and feet however does not appear to be significantly different for diabetic population as compared to control\textsuperscript{29}. 
Patient with uncontrolled diabetes with ketosis may be predisposed to deep mycotic infections such as the rare but serious rhinocerebral mucormycosis. 75-80% occur in patients with DM\textsuperscript{98}, with diabetic ketoacidosis being the most important risk factor. Ketoacidosis blunt the normal inhibitory activity of serum against rhizopus\textsuperscript{98}. Treatment consists of aggressive debridment and intravenous amphotericin B.

Gupta et al\textsuperscript{99} demonstrated that the rate of toenail onychomycosis was 2.77 times greater in patients with DM as compared to controls. In addition they found peripheral vascular disease to be a significant predictor.

**ACANTHOSIS NIGRICANS**

This condition presents as brown to gray-black papillomatous cutaneous thickening in the flexural areas including the posterolateral neck, axilla, groin and abdominal fold. The lesion is velvety and in some instances mucosal surfaces may the involved. The commonest site is however the back of the neck.\textsuperscript{100}

Acanthosis nigricans can be associated with malignancy,\textsuperscript{101} though common in the population and mostly associated with
obesity, insulin resistance and hyperinsulinaemia.\textsuperscript{102} It is a prognostic indicator for development of type 2 DM.\textsuperscript{103}

Acanthosis nigricans in insulin resistance and hyperinsulinaemia may be due to the binding of insulin to the insulin growth factor (IGF-I) receptors on keratinocytes and fibroblasts.\textsuperscript{104} It has been shown that high levels of insulin stimulates in-vitro fibroblast DNA synthesis and proliferation through IGF-1 receptors.\textsuperscript{104}

Other associations with acanthosis nigricans include hyperandrogenic states in female,\textsuperscript{103} systemic corticosteroids, nicotinic acid and estrogens such as diethylstilbestrol.\textsuperscript{101} Treatment is ineffective, but may resolve following weight loss in obese patients.\textsuperscript{102}

Nearly 40\% of native American teenagers, 13\% of African American, 6\% of Hispanic, and less than 1\% of white, non-Hispanic children between ages of 10-19 have acanthosis nigrican, and this identifies a subgroup within an ethnic group that has the highest insulin concentration, the most severe insulin resistance, and the highest risk of the development of type 2 diabetes.\textsuperscript{105}

In the Cherokee Diabetes study, a cross sectional study of a young American Indian population, the prevalence rates of
acanthosis nigricans and hyperinsulinaemia were 34.2% and 47.2% respectively.\textsuperscript{106}

Microscopically, acanthosis nigricans is characterized by papilomatosis and hyperkeratosis.\textsuperscript{107}

Treatment of acanthosis nigricans involve addressing the underlying condition e.g. weight loss in obesity, treatment of underlying endocrinopathy, removal of casual tumour where applicable. Some specific treatments include; topical retinoids, topical calcipotriol, keratolytics eg urea and salicylic acid, insulin sensitizers e.g. metformin and rosiglitazones, systemic retinoids and laser therapy.

**DIABETIC THICK SKIN**

Patients with diabetes have thicker skin than their non-diabetic counterparts. Diabetics in general have a clinically inapparent but measurable increased skin thickness unassociated with symptoms and goes unnoticed by patients and physicians. Diabetics also have clinically apparent thickening of skin involving the fingers and hands ranging from pebbled skin to scleroderma-like skin changes. Furthermore, they may have an infrequent syndrome of diabetic scleroderma in which the patients develop markedly thickened dermis on the upper back region. This
demonstrable skin thickness have been confirmed using ultrasound. 108

Thickening of the dorsum of the hands may occur in a third of patients with diabetes.59 Rosenbloom et al reported in study of 309 mostly type I diabetics that 30% had joint limitation and one third of these had thick tight waxy skin that the examiner could not tent, mostly involving the dorsum of the hands.109 This have been confirmed by other authors and the observation extended to type2 DM.110 Limited joint movement is associated with increased duration of DM and poor glycaemic control.111,112

A longitudinal prospective study showed a 2.5 fold increase in the risk of limited joint movement for every unit increase in glycosylated haemoglobin.112 Limited joint movement directly correlate with microvascular disease.109,111

Scleredema diabeticorum was recognized in 1970 as a syndrome,113 and presents with insidious onset, painless, symmetric thickening of the skin of the upper back and neck. Spread to the face, shoulder and anterior torso may occur. The skin retains a non-pitting peau d’orange quality. Identical changes occur with post streptococcal pharyngitis, though this is sudden and the symptom remits over time.
Scleredema diabeticorum has a reported prevalence of 2.5% in patients with type 2 diabetes with a male preponderance of 10:1.\textsuperscript{114} It is a disease of long standing diabetes, associated with obesity. Most patients have type 2 DM. It has not been reported in children. Treatment for scleredema diabeticorum is usually unsuccessful. Case reports describe treatment with radiotherapy, low dose methotrexate and prostaglandin E\textsubscript{1}.\textsuperscript{115,116}

The aetiology of scleredema diabeticorum is unclear. Glycation of skin collagen and skin hypoxia due to microangiopathy may be key factors. Microscopic examination shows a thickened dermis with large swollen collagen bundles, particularly type 1 collagen, separated by ground substance and wide clear spaces. There is no inflammation of the dermis and no increase in the number of dermal fibroblasts, features which distinguish scleredema from scleroderma. There may be increased numbers of mast cells and variable expression of glycosaminoglycans. Type 1 subunits of procollagen 1 and 111 messanger RNA (mRNA) and fibronectin mRNA were elevated in fibroblasts of cultured scleredema skin.\textsuperscript{117}
ERUPTIVE XANTHOMAS

Eruptive xanthomas in the context of diabetes mellitus are accompanied by hyperlipidaemic and hyperglycaemic states. The lesions are described as waxy, yellow papules 1-4mm in diameter surrounded by an erythematous rim and usually occur on the extensor surfaces and popliteal region. The lesion occurs in crops and may coalesce into plaque over time. These lesions though asymptomatic may be the first heralder of untreated DM and severe hypertriglyceridaemia.

Histological and biochemical studies show that lipoprotein (Chylomicrons) in the blood permeate cutaneous vessel walls and accumulate in macrophages in the dermis.\textsuperscript{118}

Eruptive xanthoma can be primary or secondary. Causes of primary eruptive xanthoma include; endogenous familial hypertriglyceridaemia, familial deficiency of apoprotein C11, and lipoprotein lipase deficiency. Secondary causes include; alcohol abuse, chronic renal failure, diabetes mellitus, drugs (estrogen, corticosteroids, systemic retinoids), high caloric intake, hypothyroidism, and obesity.

DM is the most important cause of massive hypertriglyceridaemia in genetically susceptible individuals.\textsuperscript{119}
Uncontrolled DM decreases lipoprotein lipase activity, the enzyme responsible for triglyceride metabolism and the enzymatic dysfunction is proportionate to the amount of insulin deficiency and hyperglycaemia.\(^{120}\)

Treatment of hyperglycermia involves strict dietary fat restrictions and control of the underlying DM. Lipoprotein lipase activity returns to normal after treatment with long term insulin or oral glucose lowering agents.\(^{120}\) Dietary and pharmacological lowering of the circulating triglycerides to reasonable levels will result in quick resolution of eruptive lesions in 6-8 weeks. Failure to treat high triglycerides could lead to acute pancreatitis or atherosclerosis.

**NECROBIOSIS LIPOIDICA**

The initial name of this condition i.e. Necrobiosis lipoidica diabeticorum was changed because not all patients have concurrent DM.\(^{121}\) It is an uncommon manifestation of DM, occurring in about 0.3% of these patients.\(^{122}\) This skin condition is not pathognomonic of diabetes mellitus since less than two third of patients with necrobiosis lipoidica are diabetic, it has been documented to occur prior to onset of diabetes.\(^{123}\) However, any
patient who presents with necrobiosis lipiodica should be evaluated for diabetes.

Epidemiological data show that the mean age of onset is around 30 years and that necrobiosis lipoidica occurs three times more common in women than in men.\textsuperscript{121}

In a 1966 retrospective study at the Mayo clinic, of 171 patients with necrobiosis lipoidica, two third had DM at diagnosis, and another 5-10\% had glucose intolerance.\textsuperscript{124} In a 1999 study of 65 patients with necrobiosis lipoidica, only 11\% had DM after 15 years of follow up.\textsuperscript{125} The initial lesions of necrobiosis lipoidica begin as well circumscribed erythematous papules. Evolving radially, the sharply defined lesions have depressed, waxy, yellow-brown, atrophic telangiectatic centres through which underlying dermal blood vessels can be visualized. The periphery is slightly raised and erythematous and there is partial or complete anaesthesia of the lesions\textsuperscript{126}. Ulceration is reported in about one third of leg lesions, mostly in large lesions, following minor trauma. Lesions of necrobiosis lipoidica sometimes resolve spontaneously. They seem to occur and persist independent of degree of control of hyperglycaemia. The reason for this persistence cannot be readily adduced. Where most lesions of necrobiosis occur on the legs,
about 15% of lesions are found elsewhere, including the hands, forearms, abdomen, face or scalp. When necrobiosis lipoidica occurs in areas other than the lower extremities, the patient is less likely to be diabetic.¹²⁷

The histopathology of the lesion reveals neutrophilic infiltration.¹²⁸ With progression, there is collagen degeneration and destruction of adnexal structures, lesions evolve through granulomatous and sclerotic stages, with most of the sclerosis occurring in the lower reticular fatty deposits that give the lesions their yellow colour. Focal proliferation of endothelial cells encroaching upon the vascular lumina (obliterative endarteritis) has also been observed. Balloning degeneration involving isolated endothelial cells of cutaneous capillaries have also been described.

Despite the microangiopathic changes, necrobiosis lipoidica, due to its rarity, is seen only in a small minority of patients with diabetic microvascular disease. A small number of studies have documented a correlation between necrobiosis lipoidica and microvascular disease, however children with necrobiosis lipoidica have a higher frequency of persistent microalbuminuria and retinopathy than control.¹²⁹
Treatment is used to arrest the progression of the disease. This is most commonly achieved by application of high potency topical steroids or intralesional injection of steroids into the active margin. Other agents reported include pentoxifylline, and high dose oral nicotinamide. Currently the most impressive therapeutic option may be oral corticosteroids. Five weeks of oral corticosteroid treatment was described as resulting in complete disease cessation for all six patients so treated. Photodynamic therapy have also been used successfully to treat necrobiosis lipoidica.

**GRANULOMA ANNULARE (GA)**

The evidence that granuloma annulare is associated with Diabetes Mellitus is inconclusive. It presents as erythematous domed shaped papules arranged in an annular configuration in whites and flesh coloured to grey in blacks. They may form indurated circular or semicircular plaques with central clearing. There are five types of granuloma annulare; localized, generalized, perforating, subcutaneous and patch type. All age groups and races are susceptible with the higher incidence found in children and young adults. Localized form occur frequently in children and young adult. Eighty five percent of patients have fewer than 10
lesions and site of predilition include the dorsum of the hands, ankles, and feet.

The pathogenesis is largely unknown, one possible trigger is UV exposure. GA has a predilection for sun exposed areas. Other triggers are thought to include areas previously affected by herpes zoster, EBV, TB, the koebner phenomenon/trauma-induced, and insect bites. GA may represent a delayed type hypersensitivity reaction to an unknown antigen in the dermis and subcutaneous tissue. In rare cases, fascia and tendons are affected causing sclerosis.

The association of GA with DM is widely discussed and appears to be less strong than that of necrobiosis lipoidica. Although most patients are in good health, an association with DM is reported in literature, Dabski and Wilklemann reported DM in 10 of 1353 patients with localized GA and 21% of 100 patients with systemic GA.

A small retrospective case control study showed an increased prevalence of DM among patients with GA (11 of 61, 18%) as compared with the prevalence in age matched control (10 of 120, 7.2%).
Treatment is with potent topical or intralesional steroids. Treatment with systemic glucocorticoids, niacinamide, chloroquine, aspirin and potassium iodide have been reported.\textsuperscript{137} PUVA resulted in clearance in a series of one and five cases. \textsuperscript{137} Cyclosporine and Infliximab have been used in severe cases.\textsuperscript{134}

**ACQUIRED PERFORATING DISORDERS:**

The majority of patients with adult onset acquired perforating dermatosis have kidney failure associated with diabetes.\textsuperscript{138} This condition is not limited to diabetic patients and may occur in patients with other forms of kidney disease, as well as in hypothyroidism, hyperparathyroidism, lymphoma, AIDS, and liver disease.\textsuperscript{139} Itching and scratching accompany this entity, also known as kyrle’s disease or reactive perforating collagenosis. The lesions are located primarily on the extremities but can occur on the face and trunk. The lesions are described as a few millimeters in diameter, papular, often with a keratotic plug, and are often intensely pruritic. Another feature consists of elimination of collagen and elastin throughout the affected epidermis.

Although the cause of kyrle’s disease appears to be an inflammatory reaction, microvasculopathy has been noted in the underlying dermis of biopsy specimens.\textsuperscript{140} Histologic examination
reveals an invaginated atrophic epidermis surrounding a plug of degenerated material, which has elements of leukocytes, collagen, elastin, and nuclear debris.\textsuperscript{141}

Acquired perforating disorder is difficult to treat. Retinoic acid has shown some benefit along with topical antihistamines to alleviate pruritus. \textsuperscript{142}

**BULLOSIS DIABETICORUM**

A bullous eruption particular to diabetes was first described in 1930.\textsuperscript{143} Diabetic bullae are usually confined to the hands and feet. The blister are distinct, occur spontaneously, non-inflammatory and mostly non-scarring. The lesions tend to be painless and asymptomatic, but occasional mild discomfort or burning sensation has been reported, and healing occurs spontaneously within 2-6 weeks. Patients tend to have adequate circulation in the affected extremities but have signs of diabetic neuropathy. There are three types of diabetic bullae. The most common type is sterile and fluid containing and heals without scarring. Histology shows intraepidermal cleavage without acanthosis, subepidermal separation of the epidermis from the dermis can also occur.\textsuperscript{59} Bullae with subepidermal separation are often associated with diabetic nephropathy. The second type is
haemorrhagic and heals with scarring. The third type involves multiple non-scarring bullae on sun-exposed, tanned skin. One study mentioned an association with long standing type I DM. The pathogenesis of these lesions has not been clearly elaborated.

Bullosis diabeticorum is a rare condition, with only few cases having been reported in the literature. The patients have long standing diabetes or multiple complications of diabetes. Male to female ratio is 2:1 with an age range of 17-79 years, mostly elderly. Unlike the bullae of pemphigoid and pemphigus, there is no evidence of immunoglobulin deposition.

**PRURITUS**

Although it has been said that diabetes mellitus is a cause of generalized pruritus there is little evidence that this is so. What is common, however is localized pruritus, particularly of the vulva, perianal skin and lower extremities, the cause of which is usually infection by candida or dermatophyte fungi or excessive dryness of the skin secondary to anhidrosis or oligohidrosis due to diabetic neuropathy. Neily et al in a study of 300 diabetic patients found generalized pruritus without apparent cause in only 8 patients (2.7%) and thus concluded that this was not significantly more common than in the non-diabetic population. Onunu et al
found generalized pruritus in 4.8% of diabetics and in 3.6% of non diabetic populations. However, Hajieh Shhbazien et al, and Nawat Al-Mutari et al, found generalized pruritus in 46% and 49% of diabetic population studied.

VITILIGO

This is characterized by depigmentation of skin due to loss of melanocyte. It has been reported to occur with increased frequency in diabetics. Dawber in 1966, reported a prevalence of 4.8% in 520 diabetes patients compared to 0.7% in 443 control subjects. The exact pathogenesis is still unclean, however an auto-immune process is likely because of the frequent association of vitiligo with other diseases of autoimmune origin such as hyperthyroidism and Addison’s disease. The most commonly affected site is the trunk, the legs being infrequently involved.

YELLOW SKIN

Yellow nails and skin associated with diabetes is a benign condition with no known significance. Traditionally considered to be carotinaemia, recent evaluations indicate that serum carotene levels are not elevated as they had been years ago when the standard diabetic diet involved heavy consumption of vegetables.
One possible cause of yellow skin might be glycosylation end products, 2-(2-furoyl)-4(5)-(2-furanyl)–IH–imidazole which has a yellow hue that gives the characteristic colour of yellow skin.$^{152,153}$

The yellow colour is best appreciated at the distal hallux of the nails, palms, and soles of whites and fair coloured individuals. There is no current treatment for this condition.

**SKIN TAGS**

Skin tags are small, soft, pedunculated lesions occurring in eyelids, neck and axilla. Obesity is often associated with development of skin tags.

However in a study conducted on 216 patients with skin tags by kahana et al. 57(26%) had diabetes, and only about one quarter of the diabetics were classified as obese.$^{154}$ Although obesity is often associated with the development of skin tags, this study shows that skin tags are more associated with diabetes than with obesity.

Crook$^{155}$ found that skin tags were associated with the typical atherogenic lipid profile seen in insulin resistant states: elevated triglycerides and low levels of high density lipoprotein cholesterol.

Treatment is not necessary, but skin tags can be removed with grade 1 scissors, cryotherapy, or electrodessication.$^{155}$
SKIN DISORDERS ASSOCIATED WITH INSULIN THERAPY

LIPOATROPATHY

This is usually found at the site of insulin injection, but may also involve distant sites. There is a marked female preponderance. It appears as hollowed out areas due to loss of epidermal and dermal tissue and also subcutaneous fat. Its presence correlates with high levels of circulating insulin antibodies, and immune complexes containing insulin had been demonstrated at the sites of lipoatrophy.\(^{156}\)

It is rarely seen in patients treated with only highly purified insulin. Injection well away from affected sites and dispersion of injection sites or injection of insulin combined with steroid around the edges of the atrophic areas cause them to regress.

LIPOHYPERTROPHY

This resembles a lipoma both clinically and histologically and is thought to reflect the growth factor and anabolic properties of insulin. This is because insulin tend to cause cellular growth including fat cells.
There is no evidence that the antigenicity of insulin contributes to the hypertrophy. Dispersion of insulin sites prevents the disorder from occurring.
CHAPTER FIVE

METHODOLOGY

Study Location

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.

Study population

Subjects

All consecutive DM patients attending the Medical out patient department (MOPD) of Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife who meet WHO 1999 diagnostic criteria for diabetes mellitus.

Inclusion criteria

- DM diagnosed according to the WHO 1999 diagnostic criteria for diabetes mellitus.
- Those who give informed consent to participate in the study.

Exclusion criteria

- Diabetic patients who suffer from systemic diseases unrelated to diabetes mellitus
- Patients who do not give informed consent.
Study design

The study is a descriptive cross sectional study which recruited diabetic patients attending medical outpatient department of OAUTHC, Ile-Ife.

Ethical consideration

Approval of ethics and research committee of the hospital was sought and obtained before the study (Appendix iii).

Informed consent of the patient for the study was also obtained (Appendix ii).

Sample size/Data collection method

Systematic random sampling technique was applied to collection of data.

The sample size was calculated based on documented 30% prevalence rate of cutaneous alteration among diabetics 18-21.

Sample size for descriptive cross sectional study, when studying proportion with population<10,000 is:

\[ nf = \frac{n}{1 + \frac{n}{N}} \]

\[ nf = \text{The desired sample size when population is less than 10,000} \]
\[ N = \text{The estimate of the population size} \]
\[ n = \text{The desired sample size when the population is more than 10,000} = Z^2Pq \]
\[ d^2 \]
\[ P = \text{The proportion in the target population estimated to have a particular characteristic (in this case = 0.3)} \]
\[ Z = \text{The standard normal deviation (using 95\% confidence level = 1.96)} \]
\[ d = \text{Degree of accuracy desired, set at 0.05} \]
\[ q = 1.0 - P \]
so,
\[ n = (1.96)^2 \times 0.3 \times 0.7 \]
\[ (0.05)^2 \]
\[ = 3.8416 \times 0.21 = 322.7 \]
\[ 0.0025 \]

This was rounded up to 350 to make up for possible data loss.

**Protocol I: Clinical Diagnosis**

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

Protocol II; Clinical History.

Data was obtained from the patients using proforma (Appendix i) that includes demographic data such as age, sex, occupation and educational qualification. Date of diagnosis of diabetes was obtained and duration of diabetes noted. Family history of diabetes was sought for and the type of treatment used for blood glucose control obtained. Other relevant history to suggest possible complications was sought for such as frothiness of urine for possible nephropathy, this is due to the financial constraints of doing twenty four hours urinary profile for all the patients, while renal biopsy is technically not possible for the patients, loss of or abnormal sensation in the digits for possible neuropathy and confirmed by light touch and pin prick sensation,
previous history of altered sensorium, sweating etc for possible previous diabetic emergencies.

**Protocol III;**

Thorough physical examination, during which the whole skin was examined in bright light for any abnormality was carried out.

The weight of each patient was obtained using a weighing scale and the height was obtained using a standiometer. 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 considered as overweight while >30 was considered obese.

All the patients had their blood pressure measured at least 5 minutes after sitting. Blood pressure of <140/90mmHg was taken to be normal while values equal to or greater than 140/90mmHg were taken as hypertensive.

Hand lens/magnifying glass was used where appropriate to make small tiny vascular changes, small scales and skin markings more obvious.
Protocol IV: Laboratory investigation

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 by the investigator. 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. Cultures were done for all subjects with clinical diagnosis of Tinea pedis for speciation since it was the predominant fungal infection observed. This was done by inoculating the specimens on petri dishes containing Sabouraud Dextrose Agar and covered. The dishes were incubated at room temperature for four weeks to allow for fungal growth. Microscopic examination was done thereafter to speciate the fungi. Skin biopsy for histology was also done for confirmation when indicated.
Glycated haemoglobin 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 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 done by the Diabetic Association of Nigeria (DAN) for all patients. Mean FBS and 2HPP less than 7mmol/l and 10mmol/l was considered good glycaemic control, while values greater than 7mmol/l and/or 10mmol/l was considered 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 ANALYSIS**

Data was analysed using a statistical computer soft ware SPSS 16.0

Data was represented using descriptive statistics such as tables, graphs, and charts as necessary and inferential statistic such as chi square and z-score tests. P value of less than 0.05 was used as level of significant.
CHAPTER SIX

RESULT

General characteristic of the subjects.

A total of three hundred and fifty five diabetic subjects were involved in the study. They comprised of one hundred and ninety two female (54.1%) and one hundred and sixty three male (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).
Table 1: General Characteristic of the Patients

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<td>2.3</td>
</tr>
<tr>
<td>Type 2</td>
<td>347</td>
<td>97.7</td>
</tr>
<tr>
<td>Total</td>
<td>355</td>
<td>100.0</td>
</tr>
<tr>
<td><strong>Duration of Diabetes Mellitus</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤5</td>
<td>239</td>
<td>67.3</td>
</tr>
<tr>
<td>6 – 10</td>
<td>81</td>
<td>22.8</td>
</tr>
<tr>
<td>&gt;10</td>
<td>35</td>
<td>9.9</td>
</tr>
<tr>
<td>Total</td>
<td>355</td>
<td>100.0</td>
</tr>
<tr>
<td><strong>BMI (kg/m^2)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;18.5</td>
<td>11</td>
<td>3.1</td>
</tr>
<tr>
<td>18.5 – 24.9</td>
<td>139</td>
<td>39.2</td>
</tr>
<tr>
<td>25 – 29.9</td>
<td>148</td>
<td>41.7</td>
</tr>
<tr>
<td>&gt;30</td>
<td>57</td>
<td>16.1</td>
</tr>
<tr>
<td>Total</td>
<td>355</td>
<td>100.0</td>
</tr>
</tbody>
</table>
Prevalence and pattern of dermatological lesions.

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. 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. They were present as multiple atrophic hyperpigmented shin spots.

Acanthosis nigricans was seen in twenty two (4.9%) subjects. They were seen in the axilla of the subjects especially obese female subjects. Eighteen (4.0%) subjects had diabetic thick skin, much 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 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 and erysipelas-like erythema (dark brown in blacks) were each seen in ten diabetic (2.2\%) subjects while scleroderma diabeticorum was observed in nine diabetic (2.0\%) subjects. The subjects with vitiligo had localized, acrofacial and generalized variants. The scleroderma diabeticorum were present as induration and thickening of the skin of the upper back. Idiopathic guttate hypomelanosis was seen in seven (1.6\%) subjects as multiple hypopigmented macules 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 was scalp and facial while seborrheic keratosis was found on the face and trunk in the two cases. Herpes zoster was multidermatomal 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.

Granuloma annulare, acquired perforating disorder, necrobiosis diabeticorum, and bullosis diabeticorum were not seen in any of the diabetic subjects examined.

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. Majority of the patients had interdigital Tinea pedis and more than one interdigital space was involved in most. Few subjects had plantar Tinea pedis. Also the Tinea pedis in most of the subjects have been recurrent over years,

lxxii
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%) were candida intertrigo, thirty six (10.1%) vaginal candidiasis and one (0.3%) candida paronychia. The intertrigial candidiasis were seen under the breast in obese females and the groin especially among females with vaginal candidiasis and in 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. The only cutaneous bacteria infection seen in this study was furuncles and was found in sixteen (3.6%) diabetic subjects.

Table 4 shows the prevalence of dermatophyte species responsible for Tinea pedis in diabetic subjects. Epidermophyton was the most prevalent, responsible for infection in fifty (89.2%) of the fifty six diabetic patients with Tinea pedis. Tricophyton and microsporum had similar prevalence of 5.4% as each of them was found to be responsible for infection in three of the diabetic subjects with Tinea pedis.
<table>
<thead>
<tr>
<th>Dermatological disorders</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superficial fungal infections</td>
<td>163</td>
<td>35.40</td>
</tr>
<tr>
<td>Pruritus</td>
<td>76</td>
<td>16.70</td>
</tr>
<tr>
<td>Diabetic dermopathy</td>
<td>67</td>
<td>14.80</td>
</tr>
<tr>
<td>Acanthosis nigrican</td>
<td>22</td>
<td>4.90</td>
</tr>
<tr>
<td>Diabetic thick skin</td>
<td>18</td>
<td>4.00</td>
</tr>
<tr>
<td>Bacterial infection</td>
<td>16</td>
<td>3.60</td>
</tr>
<tr>
<td>Diabetic ulcer</td>
<td>16</td>
<td>3.60</td>
</tr>
<tr>
<td>Skin tag</td>
<td>13</td>
<td>3.00</td>
</tr>
<tr>
<td>Tendinous xanthoma</td>
<td>12</td>
<td>2.60</td>
</tr>
<tr>
<td>Vitiligo</td>
<td>10</td>
<td>2.20</td>
</tr>
<tr>
<td>Erysipelas like erythema</td>
<td>10</td>
<td>2.20</td>
</tr>
<tr>
<td>Scleroderma diabeticorum</td>
<td>9</td>
<td>2.00</td>
</tr>
<tr>
<td>Idiopathic gutate hypomelanosis</td>
<td>7</td>
<td>1.60</td>
</tr>
<tr>
<td>Insulin lipohypertrophy</td>
<td>4</td>
<td>0.90</td>
</tr>
<tr>
<td>Seborrheic dermatitis</td>
<td>2</td>
<td>0.45</td>
</tr>
<tr>
<td>Seborrheic keratosis</td>
<td>2</td>
<td>0.45</td>
</tr>
<tr>
<td>Herpes zoster</td>
<td>2</td>
<td>0.45</td>
</tr>
<tr>
<td>Viral wart</td>
<td>1</td>
<td>0.23</td>
</tr>
<tr>
<td>Lichen simplex chronicus</td>
<td>1</td>
<td>0.23</td>
</tr>
<tr>
<td>Keloids</td>
<td>1</td>
<td>0.23</td>
</tr>
<tr>
<td>Insulin lipoatrophy</td>
<td>1</td>
<td>0.23</td>
</tr>
<tr>
<td>Diabetic rubeosis</td>
<td>1</td>
<td>0.23</td>
</tr>
</tbody>
</table>
Table 3: Prevalence of infections among diabetic patients (n=163)

<table>
<thead>
<tr>
<th>Infections</th>
<th>Frequency(n)</th>
<th>Percent(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fungal Infections</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tinea Infections</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tinea corporis</td>
<td>7</td>
<td>1.50</td>
</tr>
<tr>
<td>Tinea unguium</td>
<td>8</td>
<td>1.80</td>
</tr>
<tr>
<td>Tinea pedis</td>
<td>56</td>
<td>12.30</td>
</tr>
<tr>
<td><strong>Cutaneous candidiasis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Candida intertrigo</td>
<td>40</td>
<td>8.80</td>
</tr>
<tr>
<td>Vaginal candidiasis</td>
<td>36</td>
<td>7.90</td>
</tr>
<tr>
<td>Candida paronychia</td>
<td>1</td>
<td>0.23</td>
</tr>
<tr>
<td><strong>Pityriasis versicolor</strong></td>
<td>67</td>
<td>14.80</td>
</tr>
<tr>
<td><strong>Bacterial infections</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Furuncles</td>
<td>16</td>
<td>3.60</td>
</tr>
<tr>
<td><strong>Viral infection</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Viral wart</td>
<td>1</td>
<td>0.23</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>232</td>
<td></td>
</tr>
</tbody>
</table>
Table 4: Prevalence of dermatophyte species in diabetic patients with Tinea pedis (n=56)

<table>
<thead>
<tr>
<th>Species</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trichophyton</td>
<td>50</td>
<td>89.2</td>
</tr>
<tr>
<td>Microsporum</td>
<td>3</td>
<td>5.4</td>
</tr>
<tr>
<td>Epidermophyton</td>
<td>3</td>
<td>5.4</td>
</tr>
<tr>
<td>Total</td>
<td>56</td>
<td>100.0</td>
</tr>
</tbody>
</table>
Pattern of glycaemic control and its association with the presence of cutaneous lesions.

Table 5 shows the pattern of glycaemic control and its association with the presence of cutaneous lesions. One hundred and eighty three subjects (51.5%) had good glycaemic control, whereas one hundred and seventy two subjects (48.5%) had poor glycaemic control. Among the ninety six subjects without skin lesions, eighty one (84.4%) had good glycaemic control, while fifteen (15.6%) had poor glycaemic control. Two hundred and fifty nine subjects had cutaneous lesions, one hundred and two of them (39.4%) had good glycaemic control while one hundred and fifty seven (60.6%) had poor glycaemic control. There is a statistically significant association between blood glucose control and the presence of cutaneous lesion among the diabetics (p< 0.01).

Table 6 shows pattern of glycaemic control using glycated haemoglobin and its association with the presence of cutaneous lesions. One hundred and fifty seven subjects had their blood glucose assessed with glycated haemoglobin, eighty three (52.9%) subjects had good glycaemic control, the remaining seventy four (47.1%) subjects had poor glycaemic control. There is a statistically significant association between glycaemic control using glycated
haemoglobin and the presence of dermatological lesions in diabetic subjects (p<0.01).

Table 7 shows the association between infections and blood sugar control. Among the diabetic subjects with infective dermatoses, fifty seven (33.5%) had good blood glucose control, while one hundred and fourteen (66.7%) had poor blood glucose control. Among those patients without infective dermatoses, one hundred and twenty six (68.5%) had good glycaemic control, while fifty eight (31.5%) had poor blood glucose control. There is a statistically significant association between infective dermatoses and blood glucose control (p<0.01).
Table 5: Pattern of glycaemic control and its association with presence of cutaneous lesions.

<table>
<thead>
<tr>
<th>Blood sugar control</th>
<th>Cutaneous lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>State</td>
<td>Frequency (%)</td>
</tr>
<tr>
<td>Good</td>
<td>183 (51.5)</td>
</tr>
<tr>
<td>Poor</td>
<td>172 (48.5)</td>
</tr>
<tr>
<td>Total</td>
<td>355 (100%)</td>
</tr>
</tbody>
</table>

\[ X^2 = 56.766, \text{ df } = 1, \text{ P-value } = 0.000 \]
Table 6: Pattern of glycaemic control using glycated haemoglobin percentage and its association with the presence of dermatological lesions

<table>
<thead>
<tr>
<th>Glycated haemoglobin control</th>
<th>Frequency (%)</th>
<th>Absent (%)</th>
<th>Present (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good</td>
<td>83 (52.9)</td>
<td>31 (37.3)</td>
<td>52 (62.7)</td>
</tr>
<tr>
<td>Poor</td>
<td>74 (47.1)</td>
<td>7 (9.4)</td>
<td>67 (90.6)</td>
</tr>
<tr>
<td>Total</td>
<td>157 (100%)</td>
<td>38</td>
<td>119</td>
</tr>
</tbody>
</table>

$X^2 = 56.766, \text{ df } = 1, \text{ P-value } = 0.000$
Table 7: Association between infections and blood sugar control

<table>
<thead>
<tr>
<th>Infection</th>
<th>Blood sugar control</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Good</td>
<td>Poor</td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>57 (33.3)</td>
<td>114 (66.7)</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>126 (68.5)</td>
<td>58 (31.5)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>183 (51.5)</td>
<td>172 (48.5)</td>
<td></td>
</tr>
</tbody>
</table>

$X^2 = 43.832, \ df = 1, \ P\text{-value} = 0.000$
**Association of dermatological lesions and other parameters.**

Table 8 shows the association between gender and the presence of dermatological lesions. Among the two hundred and fifty nine subjects with cutaneous lesions, one hundred and eighteen (45.6%) were males and one hundred and forty one (54.4%) were females. While among the ninety six subjects without cutaneous lesions, forty five (46.9%) were males and fifty one (53.1%) were females. There was no statistically significant association between gender and the presence of cutaneous lesions (p>0.05).

Table 9 displays the association between age and presence of dermatological lesions. Among the two hundred and fifty nine diabetic subjects with cutaneous lesions, none was less than or equal to 20 years, fifteen (5.8%) were within the 21-40 years age range, one hundred and thirteen (43.6%) were within 41-60 years age range while one hundred and thirty one (50.6%) were more than 60 years. Among the ninety six subjects without dermatological lesions, two (2.1%) were less than or equal to 20 years, three (3.1%) were within the 21-40 years age range, forty three (44.8%) were within the 41-60 years age range, while forty eight (50%) were more than 60 years. There was no statistically
significant association between age and presence of skin lesion among diabetic subjects (p>0.05).

Table 10 shows an association between socioeconomic class and presence of dermatological lesions. There is no statistically significant association between socioeconomic class and the presence of dermatological lesions (p>0.05).

Table 11 shows the association between the type of diabetes mellitus and the presence of dermatological lesions. Among the two hundred and fifty nine subjects with cutaneous lesions, six (2.3%) had type 1 DM, while two hundred and fifty three (97.7%) had type 2 DM. For the ninety six subjects without cutaneous lesions, two (2.1%) had type 1 DM, while ninety four (97.9%) had type 2 DM. There was no statistically significant association between the type of DM and the presence of cutaneous lesions (p>0.05).

Table 12 shows an association between duration of diabetes and presence of cutaneous lesions. One hundred and sixty six (64.1%) subjects with cutaneous lesions have had diabetes for just less than 5 years. Sixty two (23.9%) and thirty one (12%) of diabetics with cutaneous lesions have had diabetes for 6-10 and >10 years respectively. There was a statistically significant
association between the duration of diabetes and presence of cutaneous lesions (p<0.05).

Table 13 illustrates the association between type of treatment used to control blood sugar and cutaneous lesions. Among the diabetic patients with cutaneous lesions, eleven (4.2%) were being treated with insulin, two hundred and thirteen (82.2%) with oral hypoglycaemics, thirty four (13.1%) with combination of insulin and oral hypoglycaemics, and one subject (0.4%) on diet only. Among those without cutaneous lesions, three (3.1%) were on insulin, eighty three (86.5%) on oral hypoglycaemics, ten (10.4%) on insulin and oral hypoglycaemics and none was on diet only. There was no statistically significant association between type of treatment used for blood glucose lowering and the presence of cutaneous lesions (p>0.05).

Table 14 illustrates an association between BMI and the presence of dermatological lesions. There was no statistically significant association between BMI and the presence of cutaneous lesions (p>0.05)
Table 8: Association between gender and presence of dermatological lesions

<table>
<thead>
<tr>
<th>Gender</th>
<th>Cutaneous Lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Absent(%)</td>
</tr>
<tr>
<td>Male</td>
<td>45 (46.9)</td>
</tr>
<tr>
<td>Female</td>
<td>51 (53.1)</td>
</tr>
<tr>
<td>Total</td>
<td>96 (100.0)</td>
</tr>
</tbody>
</table>

\[ X^2 = 0.049, \text{ df } = 1, \text{ P-value } = 0.825 \]
Table 9: Association between Age and presence of dermatological lesions

<table>
<thead>
<tr>
<th>Age(years)</th>
<th>Cutaneous Lesions</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Absent(%)</td>
<td>Present(%)</td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>2 (2.1)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>21 – 40</td>
<td>3 (3.1)</td>
<td>15 (5.8)</td>
<td></td>
</tr>
<tr>
<td>41 – 60</td>
<td>43 (44.8)</td>
<td>113 (43.6)</td>
<td></td>
</tr>
<tr>
<td>&gt;60</td>
<td>48 (50.0)</td>
<td>131 (50.6)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>96 (100.0)</td>
<td>259 (100.0)</td>
<td></td>
</tr>
</tbody>
</table>

$X^2 = 6.404$, df = 3, P-value = 0.094
Table 10: Association between socioeconomic class and presence of dermatological lesions

<table>
<thead>
<tr>
<th>Socioeconomic class</th>
<th>Cutaneous Lesions</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Absent(%)</td>
<td>Present(%)</td>
</tr>
<tr>
<td>Professionals</td>
<td>19 (19.8)</td>
<td>52 (20.1)</td>
</tr>
<tr>
<td>Skilled</td>
<td>8 (8.3)</td>
<td>24 (9.2)</td>
</tr>
<tr>
<td>Unskilled</td>
<td>52 (54.2)</td>
<td>117 (45.2)</td>
</tr>
<tr>
<td>Unemployed</td>
<td>17 (17.7)</td>
<td>66 (25.5)</td>
</tr>
<tr>
<td>Total</td>
<td>96 (100.0)</td>
<td>259 (100.0)</td>
</tr>
</tbody>
</table>

$X^2 = 3.071$, df = 3, P-value = 0.381
Table 11: Association between type of DM and presence of dermatological lesions

<table>
<thead>
<tr>
<th>Type of DM</th>
<th>Cutaneous Lesions</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Absent(%)</td>
<td>Present(%)</td>
<td></td>
</tr>
<tr>
<td>Type 1</td>
<td>2 (2.1)</td>
<td>6 (2.3)</td>
<td></td>
</tr>
<tr>
<td>Type 2</td>
<td>94 (97.9)</td>
<td>253 (97.7)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>96 (100.0)</td>
<td>259 (100.0)</td>
<td></td>
</tr>
</tbody>
</table>

X² = 0.017, df = 1, P-value = 0.895
**Table 12: Association between duration of diabetes mellitus and presence of cutaneous lesions**

<table>
<thead>
<tr>
<th>Duration of DM</th>
<th>Cutaneous Lesions</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Absent(%)</td>
<td>Present(%)</td>
</tr>
<tr>
<td>≤5</td>
<td>73 (76.0)</td>
<td>166 (64.1)</td>
</tr>
<tr>
<td>6 – 10</td>
<td>19 (19.8)</td>
<td>62 (23.9)</td>
</tr>
<tr>
<td>&gt;10</td>
<td>4 (4.2)</td>
<td>31 (12.0)</td>
</tr>
<tr>
<td>Total</td>
<td>96 (100.0)</td>
<td>259 (100.0)</td>
</tr>
</tbody>
</table>

$X^2 = 6.338, \ df = 2, \ P\text{-value} = 0.042$
Table 13: Association between Type of treatment and Lesions

<table>
<thead>
<tr>
<th>Type of treatment</th>
<th>Cutaneous Lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Absent(%)</td>
</tr>
<tr>
<td>Insulin</td>
<td>3 (3.1)</td>
</tr>
<tr>
<td>Oral Hypoglycaemics</td>
<td>83 (86.5)</td>
</tr>
<tr>
<td>Insulin +oral hypoglycaemic</td>
<td>10 (10.4)</td>
</tr>
<tr>
<td>Diet only</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Total</td>
<td>96 (100.0)</td>
</tr>
</tbody>
</table>

$X^2 = 1.159$, df = 3, P-value = 0.763
### Table 14: Association between BMI and Lesions

<table>
<thead>
<tr>
<th>BMI</th>
<th>Cutaneous Lesions</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Absent(%)</td>
<td>Present(%)</td>
<td></td>
</tr>
<tr>
<td>&lt;18.5</td>
<td>5 (5.2)</td>
<td>6 (2.3)</td>
<td></td>
</tr>
<tr>
<td>18.5-24.9</td>
<td>35 (36.5)</td>
<td>104 (40.2)</td>
<td></td>
</tr>
<tr>
<td>25 – 29.9</td>
<td>45 (46.9)</td>
<td>103 (39.8)</td>
<td></td>
</tr>
<tr>
<td>≥30</td>
<td>11 (11.5)</td>
<td>46 (17.8)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>96 (100.0)</td>
<td>259 (100.0)</td>
<td></td>
</tr>
</tbody>
</table>

\[ X^2 = 4.716, \text{ df } = 3, \text{ P-value } = 0.194 \]
Complications of diabetes and their association with dermatological disorders.

Table 1 displays the prevalence of complications of diabetes mellitus. Hypertension was the complication with the highest prevalence and was seen in two hundred and thirty six (66.5%) of diabetic subjects in this study. Next to hypertension was neuropathy seen in two hundred and three (57.2%) of diabetic subjects. Other complications including hyperglycaemic emergency, ischaemia (peripheral vascular disease), and hypoglycaemic episodes were seen in fifty nine (16.6%), ninety nine (27.9%), twenty one (5.9%) of the diabetic subjects.

Table 16 shows the association between neuropathy and the presence of cutaneous lesions. Among the diabetic subjects with cutaneous lesions, one hundred and fifty two (58.8%) had neuropathy while one hundred and seven (41.3%) did not have neuropathy. There was no statistically significant association between neuropathy and the presence of skin lesions (p>0.05).

Table 17 shows the association between hypertension and the presence of cutaneous lesions. Hypertension was seen in one hundred and eighty one (69.9%) of subjects with cutaneous lesions,
but was absent in seventy eight (30.1%) of such patients. Fifty five (57.3%) of subjects without cutaneous lesions had hypertension while forty one (42.7%) did not have hypertension. There was a statistically significant association between hypertension and the presence of cutaneous lesions (p<0.05)
<table>
<thead>
<tr>
<th>Complications</th>
<th>Frequency(n)</th>
<th>Percent(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuropathy</td>
<td>203</td>
<td>57.2</td>
</tr>
<tr>
<td>Hypertension</td>
<td>236</td>
<td>66.5</td>
</tr>
<tr>
<td>Hyperglycaenic emergency</td>
<td>59</td>
<td>16.6</td>
</tr>
<tr>
<td>Hypoglycaemia</td>
<td>21</td>
<td>5.9</td>
</tr>
</tbody>
</table>
Table 16: Association between Neuropathy and the presence of cutaneous lesions

<table>
<thead>
<tr>
<th>Neuropathy</th>
<th>Cutaneous Lesions</th>
<th>Absent(%)</th>
<th>Present(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td></td>
<td>51 (53.1)</td>
<td>152 (58.8)</td>
</tr>
<tr>
<td>Absent</td>
<td></td>
<td>45 (46.9)</td>
<td>107 (41.3)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>96 (100.0)</td>
<td>259 (100.0)</td>
</tr>
</tbody>
</table>

$X^2 = 0.885$, df = 1, P-value = 0.347
Table 17: Association between Hypertension and the presence of cutaneous lesions

<table>
<thead>
<tr>
<th>Hypertension</th>
<th>Cutaneous Lesions</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Absent(%)</td>
<td>Present(%)</td>
</tr>
<tr>
<td>Present</td>
<td>55 (57.3)</td>
<td>181 (69.9)</td>
</tr>
<tr>
<td>Absent</td>
<td>41 (42.7)</td>
<td>78 (30.1)</td>
</tr>
<tr>
<td>Total</td>
<td>96 (100.0)</td>
<td>259 (100.0)</td>
</tr>
</tbody>
</table>

$X^2 = 4.984$, df = 1, P-value = 0.026
FIGURE 1: INTERDIGITAL TINEA PEDIS
FIGURE 2: PLANTAR TINEA PEDIS
FIGURE 3: FURUNCLES
FIGURE 4: VAGINAL CANDIDIASIS
FIGURE 5: DIABETIC DERMOPATHY
FIGURE 6: ACANTHOSIS NIGRICAN
FIGURE 7: TENDINOUS XANTHOMA
FIGURE 8: VITILIGO
FIGURE 9: SKIN TAG
FIGURE 10: SCLEREDEMA DIABETICORUM
FIGURE 11: DIABETIC THICK SKIN WITH PRAYER SIGN
H&E x 6.3 Section shows skin tissue with hyperpigmentation of stratum basalis. There is focal lymphocytic infiltration of the reticular dermis.
Scleredema Diabeticorum – Low Power

H&E x6.3 shows broad bands of collagen bundles separated by clear fenestration
H&E x40 Section shows the reticular dermis with collagen bands separated by clear spaces.
LABORATORY REQUEST FORM  
(HISTOPATHOLOGY/CYTOLOGY)

<table>
<thead>
<tr>
<th>HOSPITAL NO: 293286</th>
<th>HISTOLOGY/CYTOLOGY NO. H92/11</th>
</tr>
</thead>
<tbody>
<tr>
<td>SURNAME</td>
<td>OTHER NAMES</td>
</tr>
<tr>
<td>WARD/CLINIC</td>
<td>Dermatology</td>
</tr>
<tr>
<td>CONSULTANT IN CHARGE</td>
<td>Prof. Onayemi</td>
</tr>
</tbody>
</table>

MACRO: Received a fragment of greyish white tissue partially covered by negroid skin, measuring 0.6x0.1x0.1cm. (AE)

MICRO: Section show skin tissue covered by intact epidermis composed of keratinizing stratified squamous epithelia with hyperpigmentation of the stratum basalis. The reticular dermis is greatly thickened with bundles of collagen fibres. These collagen fibres are broadened and are abnormally separated by clear spaces (dermal fenestration). Also seen are few fibroblasts within the reticular dermis. There is dense fibrosis of the papillary dermis with scanty infiltration by inflammatory cells mainly lymphocytes.

DIAGNOSIS: Skin Biopsy: Feature Consistent with Scleroderma
No evidence of malignancy

Dr. A.E. Omonisi

PATHOLOGIST: Dr. A.O. Komolafe
7th February, 2011
(H&E x6.3 objective) section shows tissue composed of foamy histiocytes with small centrally placed nuclei and apparently clear cytoplasm with caliber vascular channels.
H&E x25 objective. Section shows foamy histiocytes with clear finely granular cytoplasm
H&E x40 objective. Showing foreign body giant cells reaction and myxoid fibrocollagenous stroma.
MACRO: Received an irregularly shaped and encapsulated tissue with fibrous tissue attached. This tissue measures 4.5x1x1 cm. Cut surfaces shows a solid and creamy tissue. (AE)

MICRO: Sections show an encapsulated tissue composed of aggregates of multinucleated giant cells mixed with histiocytes and lymphocytes. The stroma basically consists of a densely collagenous fibrous tissue and admixed are elongated fibroblasts with considerable areas of fibrosis.

DIAGNOSIS: Left Index Finger Mass: Feature are Consistent with Xanthoma Tuberosum
No evidence of malignancy.
CHAPTER SEVEN

DISCUSSION

This study shows that diabetic patients are prone to developing dermatological disorders. 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\(^{62}\) found a prevalence of 68%, Hajieh et al\(^{64}\) and Khurshid et al\(^{157}\) established a prevalence of 92% and 76.6% respectively in their research work on diabetics while Onunu et al\(^{30}\) 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.

The sex distribution of the subjects showed a male:female ratio of 1:1.2 which is similar to that of Khurshid et al\(^{157}\) who studied 350 diabetics and is comparable to the 1:1.38 documented by Mahajan S et al.\(^{158}\) In this study there was no statistically significant difference between male and female subjects, showing that DM is not gender specific.
The population of diabetics in the study had a mean age of 59.76 years and a range of between 16 – 87 years. This age distribution is similar to the mean age of 56.40 years and range of 18 – 83 years reported by Mushkoor et al \(^6\), mean of 54 reported by Khurshid Ahmed et al\(^{157}\), and a mean of 51 years with range of 9 – 80 years reported by Hajieh Shahbazian et al.\(^6\) The reason for this is likely due to the fact that majority of the patients in the various studies including this study had type 2 diabetes which is known to be very common in middle aged and elderly individuals. This latter observation may also account for the significantly higher proportion of type 2 than type 1 diabetes in this study as well as studies by Khurshid Ahmed et al\(^{157}\) and Talat Naheed et al.\(^{158}\). It is noteworthy that these studies were all carried out in the developing countries where the prevalence of type 2 diabetes mellitus is significantly out of proportion when compared to type 1 diabetes mellitus. It is possible for instance that in developing countries where infections, poverty, ignorance and lack of good health care are prevalent, patients with type 1 diabetes mellitus, a disease common in the young, would more likely succumb to the disease earlier than patients with type 2 diabetes mellitus, a disease common in middle age.
In this study 57.8% of the subjects have their BMI categorized as overweight and obese. Onunu et al.\textsuperscript{30} reported that 50.2% of their subjects fell under similar BMI category. The reason for this may be because type 2 DM is the most common type in this study and is closely associated with obesity.

Ninety point one percent of the patients in this study had been diabetic for less than 10 years while only 9.9% had been diabetic for more than 10 years. In another study by Khurshid Ahmed et al.\textsuperscript{157} 60.9% of subjects have had DM for less than 10 years while 39.1 for more than 10 years. Nawaf Al-mutari et al.\textsuperscript{61} reported 44.3% of their patients to had been diabetic for less than 10 years while 55.7% for more than 10 years. This could be pointing to possible high mortality amongst diabetics in our population, resulting in our diabetic out-patients clinic to be populated by patients who had been diabetic for relatively short time and with few long term survivors.

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.\textsuperscript{30} where infection had the highest
prevalence, accounting for 38.8% of dermatoses seen in a diabetic population. Nawaf Al-mutari et al \(^6\) found infection in 67.2% of their study population, while Mashkoor et al \(^6\) 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 high prevalence of infection in this study with p<0.01. Infections thrive in a setting of poor glycaemic control and opportunistic organism, like candida albican, 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 Nawaf et al\(^6\) where it was also the commonest of dermatophytes with a prevalence of 21%. Trichophyton accounted for the most common dermatophyte specie and was the cause of Tinea pedis in 89.2% of those infected in this study. This is
consistent with finding in another study by Muhammed Al Hassan et al \cite{160} where it accounted for 76\% of T. pedis infection. Epidermophyton accounted for 5.0\% of T. pedis in the quoted study of Muhammed Al Hassan et al \cite{160} and this finding is almost the same as the finding in this study where Epidermophyton accounted for 5.4\% of T. pedis infection. Diabetics are at an increased risk of T. pedis because of high prevalence of dry skin in them which predisposes to interdigital 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 poor glycaemic control. Herpes zoster can occur among diabetic where poor glycaemic control can cause 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.\cite{30,61,64,149} In this study, pruritus was seen in 16.7\% of subjects. This high prevalence of pruritus could possibly be because of fungal infections in diabetes which can predispose to localised itching.
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.107 Nawaf Al-mutari et al 61 and Mashkoor et al, 62 reported acanthosis nigricans in 4.7% and 11.64% of their study populations respectively. The prevalence of acanthosis nigricans in this study is therefore similar to the findings in other studies and 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 scleroderma diabeticorum were seen in 4.0% and 2.0% of patients respectively in this study. Rosenbloom et al109 reported thick skin in 33.3% of type 1 diabetics with joint limitation. Scleroderma diabeticorum was however reported in 2.5% of patients with type 2 DM116, 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.109 The prevalence of diabetic ulcer in this study was 3.6%. Osuntokun et al24 and Adetuyibi et al25 reported diabetic ulcer in 3.0 and 3.8% of their study
populations respectively. Neuropathy, peripheral vascular disease, 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, Nawaf Al-mutari et al, and Khurshid Ahmed et al. 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 and Khurshid et al. Diabetes mellitus is an important cause of acquired dyslipidaemia especially hypertriglyceridaemia which predisposes to xanthomas.

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. Dowber reported a prevalence of 4.8% among 520 diabetic patients. Though the prevalence is low, it is possible that vitiligo occurred in some diabetic patients with shared autoimmune aetiology. 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.\textsuperscript{30} 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 literature was 59%.\textsuperscript{73} 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 colour.

Glycaemic control using average of monthly blood glucose for three months and glycated haemoglobin 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\textsuperscript{157} and others,\textsuperscript{32,33} 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.

Majority of the patients with skin lesions had diabetes for less than 5 years. It was observed that there was a significant association between the duration of diabetes and skin lesions (p <0.05). Mashkoor et al\textsuperscript{62} had earlier reported a finding similar to that documented in this study whereby majority of cutaneous lesions seen were observed among patients who had been diabetic for 1-5 years. This finding may be incidental, but could be attributed to the fact that majority of the patients in this study
(67.5%) had been diabetic for less than 5 years as well. To infer that because they had been diabetic for a relatively short duration and might not have mastered the balance between medication and diet to achieve optimal glycaemic control would be conjectural since it is assumed that adequate counseling and education about their condition must have taken place before commencement of medication.

This study did not demonstrate any association between gender, type of diabetes, age and occupation with occurrence of cutaneous disorder. This is similar to the finding by Onunu et al\textsuperscript{30} where there was no association between sex, type of DM, family history of DM, and educational status of patients with occurrence of cutaneous lesions.

The prevalence of complications such as neuropathy, and hypoglycaemia in this study were similar to those reported by other workers.\textsuperscript{32,33} Neuropathy, hypertension differ, but were similar to finding by Talet Nahhed et al\textsuperscript{160} and Nawaf Al-Mutari et al.\textsuperscript{61} These complications of diabetes including neuropathy and hypertension were more prevalent among patients with cutaneous lesions than those without any lesion. However only hypertension showed a statistically significant association with cutaneous lesions (p<0.05).
This finding was similar to that by Talet Naheed et al\textsuperscript{159}, though in that study none of the complications showed any statistically significant association with cutaneous lesions. This could be due to the fact that infection which is the most common of cutaneous disorders can occur at any time in the course of DM, while most of the systemic complications are common with long standing diabetes. However the statistically significant association with hypertension could be because hypertension can occur as a result of vascular complications of DM, and cutaneous lesions are also common amongst diabetics with vascular complications, but may also be due to the fact that hypertension associated with dyslipidaemia, and with atherosclerosis could lead to poor skin perfusion with predisposition to cutaneous lesions, due to accompanying microvascular and macrovascular complications.
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. The finding of many infectious dermatoses is similar to reports by workers from other parts of the world.

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

Other complications associated with diabetes such as hypertension and neuropathy are common and were observed in this study.

Multiple infective lesions in patients who are already diabetic will suggest poor glycaemic control.
RECOMMENDATIONS

This study has demonstrated that cutaneous disorders are common among diabetics. The following are thus recommended:

1. General and thorough skin examination of every diabetic should be routinely undertaken at first presentation and as appropriate thereafter by attending physicians so that any dermatological lesions could be detected early and treated appropriately.

2. Physicians caring for diabetics should aim for optimal blood sugar control for all diabetic patients since poor glycaemic control is the single most important determinant of the presence of skin lesions in this study.

3. Appropriate education of diabetic patients should be further encouraged and it should include the need for foot care and regular feet examination. This will assist in the early detection of Tinea pedis which is predominant in such population and may be the nidus for bacterial infection that can cause non-healing ulcer with its attendant risk of amputation.
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APPENDIX 1 : QUESTIONNAIRE
DERMATOLOGICAL DISSORDERS AMONG DIABETICS AT
OAUTHC, ILE-IFE

1. Hosp No: .................................................................
2. Age: ...........................................................................
3. Sex: ............................................................................
4. Occupation: ...............................................................
5. Date of diagnosis: ......................................................
6. Duration of diabetes ..................................................
7. Educational qualification
   a. Non ..............................
   b. Primary ......................
   c. Secondary .................
   d. Tertiary ......................
8. Family history of DM
   a. Yes
   b. No
9. Type of treatment
   a. Insulin
   b. Oral hypoglycemic agent e.g
      Sulphonyuria/Bigunides/T2D/others
   c. Insulin + oral hypoglycemic agents
10. Complications of Diabetes (Historical/examination)
   a. Nephropathy
   b. Neuropathy
   c. Retinopathy
   d. Hypertension
   e. Hyperglycaemic emergencies
   f. Hypoglycemia
   g. Infections
   h. Ischaemia

11. Any other associated condition

12. Dermatological lesions
   a. No lesion
   b. Diabetic dermopathy
   c. Diabetic rubeosis
   d. Diabetic ulcer
   e. Erysipelas – like erythema
   f. Fungal infections
      i. Tinea infection
      ii. Candidiasis
      iii. Pityriosis vesicolour
g. Bacteria infections
  i. Furuncles
  ii. Any other (specify)

h. Acanthosis nigricans
  i. Diabetic thick skin

j. Eruptive xanthoma

k. Necrobiosis lipodica

l. Acquired perforating disorder

m. Bullosis diabeticorum

n. Pruritus

o. Vitiligo

p. Yellow skin

q. Insulin related disorders
  i. Lipoatrophy
  ii. Lipohypertrophy

13. Weight..................................................................................

14. Height..................................................................................

15. BMI.....................................................................................

16. Investigations
  a. FBC.................................................................................
  b. Urinalysis
i. Protein

ii. Glucose

c. FBS (Average of last 6 months) ..............................................

d. 2HPP (Average of last 6 months)...........................................

e. S/E/Ur/Cr..............................................................................

...

f. Lipid

profile.....................................................................................

g. Mycological

study.....................................................................................

h. Bacteriological

study.....................................................................................

i. Histology of skin biopsy.........................................................

APPENDIX II

INFORMED CONSENT SHEET
PATTERN OF DERMATOLOGICAL DISORDERS AMONG DIABETIC PATIENTS IN OBAFEMI AWOLOWO UNIVERSITY TEACHING HOSPITAL COMPLEX, ILE-IFE, NIGERIA.

Clients Agreement

I have read the information provided above/ have had it read to me. I have had the opportunity to ask questions have been answered to my satisfaction. I agree that blood investigations as outlined in the proforma be carried out me with collection of 5mls of my blood. I also agree that small part of my skin be cut out or scrapped (skin biopsy and scrapping) for investigations. I have the right to withdraw from the study at anytime.

Yes………………………………………… No……………………………………

................................................................. ........................................
Signature/Thumb print of research respondent Date

................................................................. ........................................
Signature/Thumb print of person obtaining consent Date

.................................................................
Name of person obtaining consent
CLEARANCE CERTIFICATE

RB/EC NUMBER: 00005422

PROTOCOL NUMBER: ERC/2008/10/03

PROJECT TITLE: PATTERN OF DERMATOLOGICAL DISORDERS AMONG DIABETIC PATIENTS IN OAUTC, ILE-IFE.

INVESTIGATOR(S) DR. O.I. EZEJIOFOR

DEPARTMENT/INSTITUTION Department of Dermatology and Venereology, Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife.

DATE CONSIDERED 30-10-2008

DECISION OF THE COMMITTEE Approved

CHAIRMAN: Professor E.O. Ogumbode SIGNATURE & DATE: 30/10/2008

Supervisor: Prof. O. Onayemi

DECLARATION BY INVESTIGATOR(S)

PROTOCOL NUMBER (Please quote in all enquiries): ERC/2008/10/03

To be completed in four and three copies returned to the Secretary, Ethics and Research Committee, Clinical Services and Training Section, Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Nigeria.

I/We fully understand the conditions under which I am/we are authorized to conduct the above-mentioned research and I/we guarantee that I/we will ensure compliance with these conditions. Should any departure be contemplated from the research procedure as approved, I/we undertake to resubmit the protocol to the Ethics and Research Committee.

Signature Date 11/11/08

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