SKIN MICROANGIOPATHY AND OTHER SKIN LESIONS IN DIABETIC PATIENTS

THESIS

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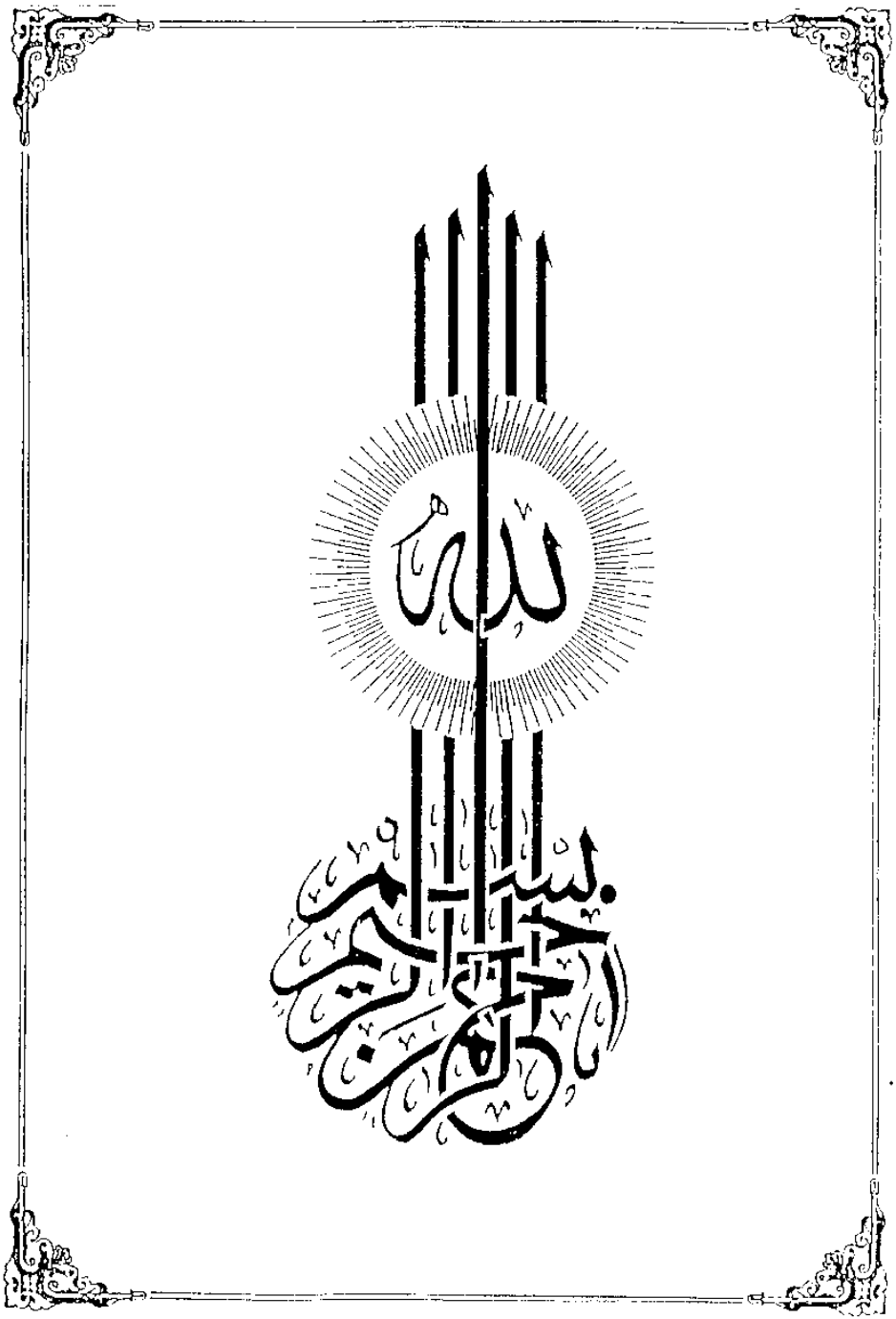

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INTRODUCTION

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Idiopathic or primary diabetes mellitus is a chronic disorder of carbohydrate, fat and protein metabolism characterised in its fully expressed clinical form by an absolute or relative insulin deficiency, fasting hyperglycaemia, glycosuria and a striking tendency towards development of atherosclerosis, microangiopathy, nephropathy and neuropathy **(Robbins et al., 1984).**

Although diabetic retinopathy was first recognized over 100 years ago, further elucidation of the nature of diabetic microangiopathy was extremely slow until the discovery of insulin in 1922. With the increased longevity of insulin treated diabetics, degenerative vascular disease gained increasing significance **(Bloodworth, 1963).**

One of the most consistent anatomic features of diabetes is diffuse thickening of basement membranes. The thickening is most evident in the capillaries of the skin, skeletal muscles, retina, renal glomeruli... etc; giving rise to the characteristic diabetic microangiopathy. In addition, a variety of skin lesions occur in long term diabetics, the commonest is infection, necrobiosis lipoidica diabeticorum, and diabetic xanthomas **(Robbins et al., 1984).**

Cutaneous capillary abnormalities; in diabetic patients, have been investigated by **Handelsman et al. (1962)** to provide information about the incidence of the capillary abnormality relative to the duration of the disease. Dermal manifestations on the lower extremities of diabetics referred to as "cutaneous atrophy", have been reported by **Melin (1964)** and termed "diabetic dermopathy" by **Binkley (1965).** Meanwhile **Danowski et al. (1966)** attributed the presence of "shin spots" in diabetics due to increase in the number of capillaries, fibroblastic proliferation and small amount of haemosiderin. **Bauer et al. (1966)** found "pigmented pretibial patches" on the skin in about 17% of mature-onset diabetics compared to their presence in about 3% of non-diabetic adults.

Brenner (1986) described several skin lesions that precede the actual clinical and laboratory diagnosis of diabetes by several months to several years. Podiatrists may well be the first physicians to see these prodromal dermopathies and be able to make an early diagnosis and aid the patients in obtaining early treatment.

AIM OF THE WORK

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The aim of this work is to study the different histopathological changes of the skin in diabetics with special reference to skin microangiopathy.

A correlative study between the histopathological findings and the clinical data; including the duration of the disease and presence or absence of complications will also be done.

REVIEW OF LITERATURE

HISTOLOGY OF THE SKIN

According to **Ham and Cormack (1979)** the integumentary system is composed of three anatomically distinct layers. From the surface downwards, these are the epidermis, the dermis and subcutaneous fat.

The epidermis:

It is the superficial layer of the skin. It is formed of stratified squamous keratinized epithelium consisting of different types of cells.

These cells are:

1. Keratinocytes
2. Melanocytes
3. Langerhans' cells
4. Merkel cells.

1. **The Keratinocytes:**

These cells arise embryologically from the ectodermal tissue and represent about 85% of the epidermal cells.

Keratinocytes form several layers which ultimately become keratinized and are continuously shed at the top layer.

The layers are:

A) Basal cell layer: [Stratum germinativum or germinal layer]

It includes a single row of vertically arranged regular columnar

cells. The cytoplasm is deeply basophilic, rich in ribosomes and polysomes, and the nuclei are deeply stained, basal and oval. These cells are connected with each other and with the overlying spinous cells by desmosomes.

The bases of these cells rest on a basement membrane and are anchored to it by hemidesmosomes.

The basal cells contain melanin pigments which parallel the skin colour.

The function of these cells is reproduction or regeneration where they undergo mitosis.

B) Prickle cell layer: [Stratum spinosum]

It includes polyhydral cells with central large rounded nuclei. They usually form 4 to 10 layers thick. They become flattened towards the surface.

The cell borders are separated by small spaces traversed by fine spine-like processes: these give the prickly appearance and account for the name of the layer. However, these are cytoplasmic processes which are joined to those of neighbouring cells by desmosomes.

This minimal intercellular substance allows the nutrients and waste products to diffuse between the more superficial living cells and the capillaries of the dermis.

Polarizing microscope reveals in the cytoplasm of the cells, numerous doubly refractile tonofibrils which do not pass from

one cell into another but they are always contained in cytoplasm. These tonofibrils contain sulph-hydral and disulphide groups **(Montagna and Parakkal, 1974).**

C) Granular cell layer: [Stratum granulosum]

It includes diamond shaped or flattened cells. It varies in thickness but more abundant in Palms and Soles. The cytoplasm is filled with deeply basophilic keratohyalin granules, variable in size and shape.

In contrast to tonofibrils, keratohyalin granules do not contain sulphydral groups.

Degeneration of the cells starts to occur in the more superficial cells.

D) Clear layer: [Stratum lucidum]

This layer consists of the protein eleidin which is supposed to be a transformation product of the keratohyalin. This part is most prominent in areas where the horny layer is thick, like in Palms and Soles.

E) Horny layer: [Stratum corneum]

It consists of several layers of acidophilic horny scales called squames. This layer is formed by the cells being pushed superficially. The keratohyalin granules fade away suggesting intracellular activity of lysosome-derived enzymes.

The squames are firmly adherent to one another by remnants of desmosomes.

2. **Melanocytes:**

These are large dendritic cells disposed beneath the cells of the basal layer of the epidermis.

Before they become functioning, they may appear as "clear cells" in H&E sections, located near the basement membrane. Functioning melanocytes can only be distinguished by "Dopa reaction". This reaction is also helpful in demonstrating the cell processes that extend from the cell bodies to interwine with the epidermal cells and inject them with pigment.

3. **Langerhans' cells:**

These cells are also dendritic, resembling melanocytes in H&E sections but are found in the upper Malpighian layer; high level clear cells (**Lever and Schaumburg-Lever, 1975**). The cells contain lysosomes and lipid droplets. Linear structures with striations and rounded ends are found in Langerhans' cells and are called "Langerhans' granules". They were thought to be old melanocytes, but E/M showed that they are healthy active cells (**Ham and Cormack, 1979**).

Breathnach and Wyllie (1965) discovered the ability of these cells to phagocytose.

Ham and Cormack (1979) considered them as dermal macrophages.

4. Merkel Cells:

These are modified cells found in the basal cell layer. They are slightly larger than the other cells but attached to them by desmosomes. They are sensory receptors commonly found in the epidermis of the Soles and Palms. Non-myelinated terminal branches of myelinated afferent nerve fibres, each penetrate the basal layer of the epidermis, lose their investment of Schwann cells and become expanded into a terminal disk attached to the base of a Merkel cell **(Ham and Cormack, 1979).**