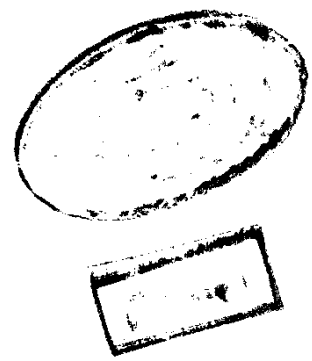
STUDY OF SOME OPPORTUNISTIC PARASITIC INFECTION IN DIABETIC PATIENTS

(TOXOPLASMOSIS - STRONGYLOIDIASIS - GIARDIASIS)



THESIS

SUBMITTED FOR PARTIAL FULFILMENT

OF THE MASTER DEGREE IN

MEDICINE

BY

SAMUEL MAKRAM AGAIBI

M.B., B.Ch.

Ain Shams University

SUPERVISED BY

Prof. Dr SAAD ABDEL MAGID FARRAG

Prof. of Internal Med. & Endocrinology

Faculty of Medicine

Ain Shams University

Prof. Dr. TOSON ALY MORSY

Prof. of Parasitology

Faculty of Medicine

Ain Shams University

FACULTY OF MEDICINE

AIN SHAMS UNIVERSITY

(CAIRO)

1987

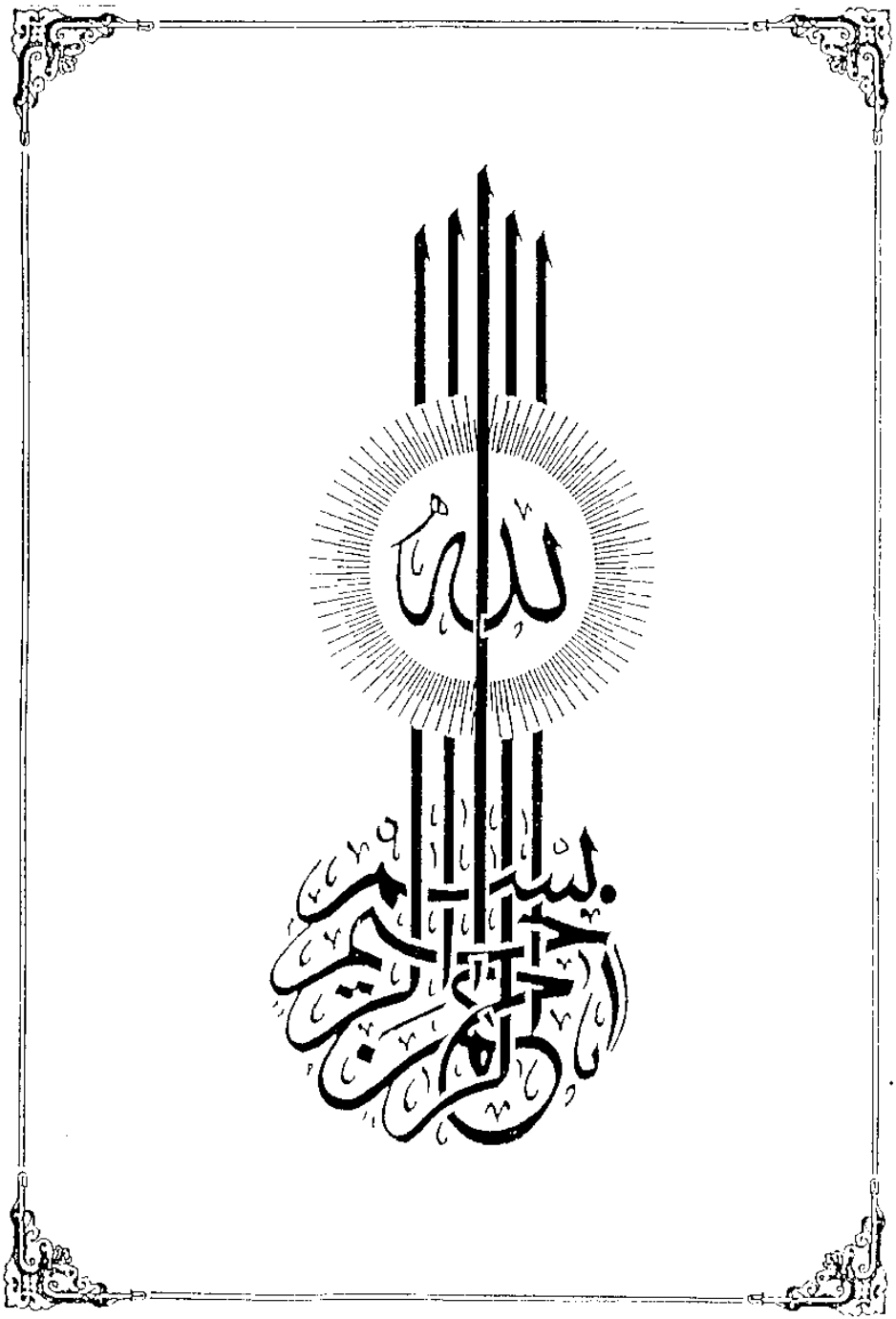
ACKNOWLEDGEMENT

Many thanks are due to Professor Dr. **Saad Abdel Magid Farrag,** Professor of Internal Medicine and Endocrinology, Faculty of Medicine, Ain-Shams University for his honest guidance, supervision, encouragement and revision.

The author wishes to express his deepest gratitude and appreciation to Professor Dr. **Toson Aly Morsy,** Professor of Parasitology,Faculty of Medicine, Ain-Shams University for his faithful help, advise,honest supervision and repeated revisions.

Many thanks are due to Dr. **Mohamed Ahmed Sarwat,** lecturer of Parasitology, Ain-Shams University, for his honest help, encouragement and support.

Many thanks are due to Dr. **Ahmed Onsy,** Lecturer of Parasitology, Ain-Shams University for helping and sharing in the practical work of this study.



CONTENTS

INTRODUCTION

INTRODUCTION

Diabetes mellitus is the most common of the serious metabolic diseases of human . The true frequency in the general population is difficult to ascertain because of the difference in the standard of diagnosis,however it may be about one percent. The disease is characterized by a series of hormone-induced metabolic abnormalities, by long term complications involving the eyes, kidneys, nerves, and blood vessels and by a lesion of the basement membranes demonstrated by electron microscope (Foster, 1983).

The increased frequency of infections in the diabetics are well known, but their causes have not been discovered, the opposite view is that infections are not common in well-controlled diabetics than in non diabetics (Ireland, et al., 1980).

The diabetic condition is said to decrease host resistance to infection, and acute infection is known to alter endocrinologic-metabolic status of the host (Rayfield, et al., 1982).

Sherris & Ray (1984) classified organisms as " Primary pathogens",which may initiate disease in a previously healthy individuals and "Opportunists"which are the frequent causes of diseases in the immunocompromised host or when first-line defense barriers are beached.

Many of the so-called "host factors " are known to influence the likehood that disease will occur if organisms enter the tissues, or to play a determining role in the outcome once the infection has become established. These include natural or acquired antibodies, interferon, properdin, phagocytic activity, and the level of the inflammatory response, which is generally manifested by cellular activity such as chemotaxis, phagocytosis, and release of lysozomal enzymes (Petersdorf, 1983).

In humans: alcoholism; diabetes; deficiency or absence of immunoglobulins; defect in cellular immunity; malnutrition; chronic administration of steroid hor-

mones; chronic lymphedema; ischemia; the presence of foreign bodies such as bullets, calculi or bone fragments, obstruction of a bronchus, the urethra or any hollow tube; agranulocytosis or congenital defect in bactericidal or viricidal activity; various blood dyscrasias; and many other circumstances influence the susceptibility to systemic or local infection (Petersdorf, 1983).

Defects in polymorphonuclear leukocyte functions such as chemotaxis (Mowat & Baum, 1971), phagocytosis (Bagdade, et al., 1974), intracellular bactericidal activity (Rayfield, et al., 1978), and serum opsonin activity(Rayfield, et al.,1978) have been reported in diabetic patients. Studies of cell mediated immunity by Mac-Cuish, et al., (1974) showed a decrease in lymphocyte transformation in response to phytohaemagglutinin in poorly controlled diabetics. Elder & Mc Laren (1983) and Naji, et al., (1983) showed T.lymphocyte immunoincompetence in a good number of insulin-dependent diabetes in BB-rats.

The potential of the protozoan parasite, Toxoplasma grondii, to cause fulminant infection in individuals with impaired immunologic defense mechanisms has been stressed (Remington, 1970 & 1974). Most immunosuppressed patients who develop clinically sever toxoplasmosis are likely to have been unwitting, asymptomatic carriers of the organism. However, dissiminated toxoplasmosis may not always result from reactivation of remotely acquired latent infection. "Exogenous" acquisition of the organism might well produce an acute, equally devasting illness in immunologically compromised individuals and yet cause no symptoms at all in normal subjects (Ruskin, and Remington, 1976).

Cavallazzi, (1985) described a case of neurological toxoplasmosis in a diabetic patient. By reviewing the literature on toxoplasmosis and its predisposing causes, none has reported correlation between diabetes and toxoplasmosis up till now.

Overhelming strongyloidiasis with dissimation of larvae throughout the body is being recognised increasingly in patients who are immunosuppressed either as a result of a disease, because of the administration of immunosuppressive agents, or both (Scowden, et al.,1978 and Siegman,et al.,1981).

Dissiminated strongyloidiasis is considered in any compromised host with unexplained gram-negative bacteremia, abdominal complaints, and pulmonary infiltrates with or without eosinophilia (Plorde, 1983)$_b$. Venturi & Viliotti (1984) described a case of dissiminated strongyloidiasis in a diabetic patient.

Yardley and Bayless (1967) noted certain host factors contributing to human susceptibility to giardiasis such as childhood, previous gastrectomy, malnutrition, and abnormalities in immunoglobulin.

Abd El-Lateaf (1982) examined the stools of 80 patients with diabetes mellitus and 25 control individuals, the prevalence of Giardia lamblia among diabetic patients was 21.5 percent as compared to 16 percent among the control group.

REVIEW OF LITERATURE

1) DIABETES MELLITUS

Diabetes mellitus can be defined as a disorder of metabolism of which the most obvious component is diminished ability to utilize carbohydrate,manifesting itself as hyperglycaemia, glucosuria, tendency to ketosis and typical complications (Ghaliounqui & Ghareeb, 1978).

Diabetes mellitus is not a disease in the clinical sense. It has no distinct and definable pathogenesis, etiology, invariable set of clinical findings, specific laboratory tests, or definitive and curable therapy. Rather, diabetes mellitus should be viewed as a syndrome- a clinical entity which can involve any or all of a long list of symptoms and clinical laboratory findings, which shows a variable response to therapy. Because abnormalities of glucose metabolism have been easiest to measure and where the first discovered, the major focus has been to define the disease by glucose measurements (Porte and Halter, 1981).

Diabetes mellitus can also be defined as a syndrome of chronic hyperglycaemia of various etiologies. It may present with acute symptoms that include thirst, polyuria and unexplained weight loss (classic onset) and these can progress to life threatening ketoacidosis or hyperosmolar coma. Subacute symptoms include the above, together with pruritis vulvae, balanitis and other skin infections (Welborn, 1984).

Four general areas are affected in the complete clinical syndrome and these should be considered in making a clinical diagnosis.

(1) Hyperglycaemia :

There is an abnormality of carbohydrate metabolism resulting in hyperglycaemia and often associated with accelerated fat and protein catabolism. This abnormality probably contributes to the other features but seems unlikely to be their sole cause.

(2) Large vessel disease :

There is accelerated atherosclerosis and medial calcification.

(3) Microvascular disease :

There is an abnormality of capillary basement membrane characterized by thickness and abnormal functions. These capillary related lesions are often termed microvascular or small-vessel concomitants of diabetes.

(4) Neuropathy :

These are peripheral sensory and motor defects, autonomic nervous system dysfunction, segmental demyelination and abnormalities of Schwann cells (Porte and Halter, 1981).

Classification of Diabetes Mellitus :

When diabetes is inherited, it is called essential or idiopathic, while secondary diabetes is related to some other diseases or it is precipitated by drugs. Some patients with secondary diabetes have a hereditary predisposition to develop diabetes, i.e are prediabetics. Hereditary idiopathic diabetes is classified into insulin-dependent diabetes mellitus (IDDM) and non insulin dependent diabetes mellitus (NIDDM) (Porte & Halter, 1981).

Table (1) shows the clinical characteristics of the two major types of Diabetes mellitus according to the National Diabetes Data Group (1979).

Table (1)

CLINICAL CHARACTERISTICS OF THE TWO MAJOR TYPES OF THE DIABETES MELLITUS

NIH Diabetes Data group Terminology.	Insulin dependent Diabetes Mellitus (IDDM)	Non Insulin dependent Diabetes Mellitus (NIDDM)
Age at onset	Usually less than 45 years	Usually over 30 years
Genetics	Less than 10% of first degree relatives are affected.	More than 20% of first degree relatives are affected.
HLA	Associated with HLA-B8, Dw 15 DW3 and DW4	No HLA association
Immunity	Increased incidence of auto-immune phenomenon.	No increase in autoimmune phenomenon.
Body weight	Usually lean	Usually obese
Metabolism	Ketosis prone	Ketosis resistant
Treatment	Insulin	Weight loss, may need oral agents or insulin

National Diabetes Data Group (1979).

A) Juvenile - onset - type Diabetes (JOD)
Idiopathic, type I, Insulin - dependent Diabetes Mellitus (IDDM)

Under new terminology, this will be called insulin dependent diabetes (IDD). Insulin deficiency is the most characteristic finding of this type of Diabetes mellitus. It is also characterized by, sudden onset, sever hyperglycaemia and rapid progression to ketoacidosis and death unless treated with insulin. About 50% of these patients are diagnosed before the age of 21, with a peak incidence near puberty (Porte and Halter, 1981).

Clinically patients with IDD are lean, and even after treatment there is a little tendency to obesity. Diagnosis is usually not a problem as they are almost always grossly hyperglycaemic and symptomatic with borderline or overt ketosis in the absence of insulin treatment. They do not respond to oral suphonylurea agents and at autopsy, have gross B-cell failure (Porte and Halter, 1981).

Islet cells antibody (ICA) have been reported in at least 85% of insulin dependent diabetics at the time of onset of their disease with a gradual decrement in the prevalence thereafter (Lendrum et al., 1976., Del Prete, et al., 1977 and Bottazzo, et al., 1974).

A significant association between ICA and specific HLA antigens has been reported by many authors. A persistant linking of ICA with HLA-B8 and DR3 (Morris, et al.,1976; Irvine,et al., 1977 and Del Prete, et al.,1977).

IDD is also associated with an increased risk of having autoantibodies to thyroid tissue and an increased risk of clinical Hashimoto's thyroiditis, another syndrome associated with HLA-B8 (Porte and Halter, 1981).

B) Maturity - onset Diabetes (MOD)
Idiopathic, type II, non Insulin Dependent Diabetes Mellitus (NIDDM)

Under new terminology, this will be called non-insulin dependent diabetes (NIDD). The ability to survive without ketoacidosis in the absence of insulin therapy is the distinguishing characteristic of these patients. This disease usually has a slow onset and in the begining is often asymptomatic, making it difficult to date the onset of the metabolic abnormality. Despite its clear genetic character, the clinical onset of the disease is relatively late and may not appear untill the 60's or 70's or 80's (Porte and Halter, 1981).

NIDD is usually associated with obesity (about 60-70%) and has no association with any HLA antigens. Insulinopenia is not present (except in later stages) although there is a blunted or delayed insulin response to glucose stimulus. The insulin response to argenine and to tolbutamide is normal in these individuals, so the deficiency of the B-cell receptors may be specific for glucose and/or the presence of post receptor block in the insulin stimulated pathways of intracellular glucose metabolism (Cudworth, 1976).

Patients with NIDDM may be asymptomatic for years or decades and show only slow progression of the disease. However the typical chronic associations and complications of diabetes, namely; macroangiopathy, microangiopathy, neuropathy and cataract may be seen in this type (Fajans, et al., 1978).

While insulin treatment is not necessary for survival, it is often used therapeutically and is effective. Thus all insulin-treated patients do not necessarily have insulin-dependent diabetes (Porte and Halter, 1981).

The etiology of the maturity-onset diabetes is not clear, although several factors predisposing to its appearance are known (Ghalioungui and Ghareeb, 1978).

Stages of Maturity - onset type Diabetes :

Because of one or more hereditary factors are believed to be essential parts of the disease and therefore are present at birth, an attempt has been made to separate the syndrome of maturity onset type diabetes into the clinical phases as they present themselves to the physician. Their classifications are based upon the presence or absence of hyperglycaemia or the degree of measurable carbohydrate intolerance. The separation between categories is arbitary. Such a classification does not mean to imply that an individual necessarily progresses from one stage of carbohydrate abnormality to the next. They are simply definitions which are used for communication between clinicians. Thus in the natural history of carbohydrate intolerance, progression or regression from one stage to the next (1) may never occur (2) may occur very slowly over many years, or (3) may be rapid and explosive (Porte and Halter, 1981).

1. Potential abnormality of glucose tolerance

This category is essentially theoretical in that it designates individuals who have the diabetic gene or genes but in whom there is no measurable carbohydrate abnormality. It covers the interval between conception and the time when abnormalities in glucose metabolism can be identified (Porte and Halter, 1981).

According to Ghalioungui and Ghareeb (1978), candidates to this group recruited amongst :-

(1) Healthy identical twin of diabetic persons.
(2) Obese subjects with diabetic history in blood relatives.
(3) Women with abnormal obstetric history: Large babies, repeated miscarriages and stillbirths, hydraminos, toxaemia of pregnancy, and foetal abnormalities.
(4) Subjects with diabetes like vascular or nervous manifestations : Coronary artery disease, neuropathy, impotence, peripheral vascular disease.