CRYPTOSPORIDIA AND DIARRHEA IN DIABETICS

THESIS
Submitted in partial fulfillment
for Master Degree in **Internal Medicine**

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1993

ACKNOWLEDGEMENT

I would like to express my deepest gratitude and profound thanks to Dr. Hassan El-Sayed Soliman, Professor of Internal Medicine, Ain Shams University, for his unlimited support for providing me with advice, suggestion and planning of this work.

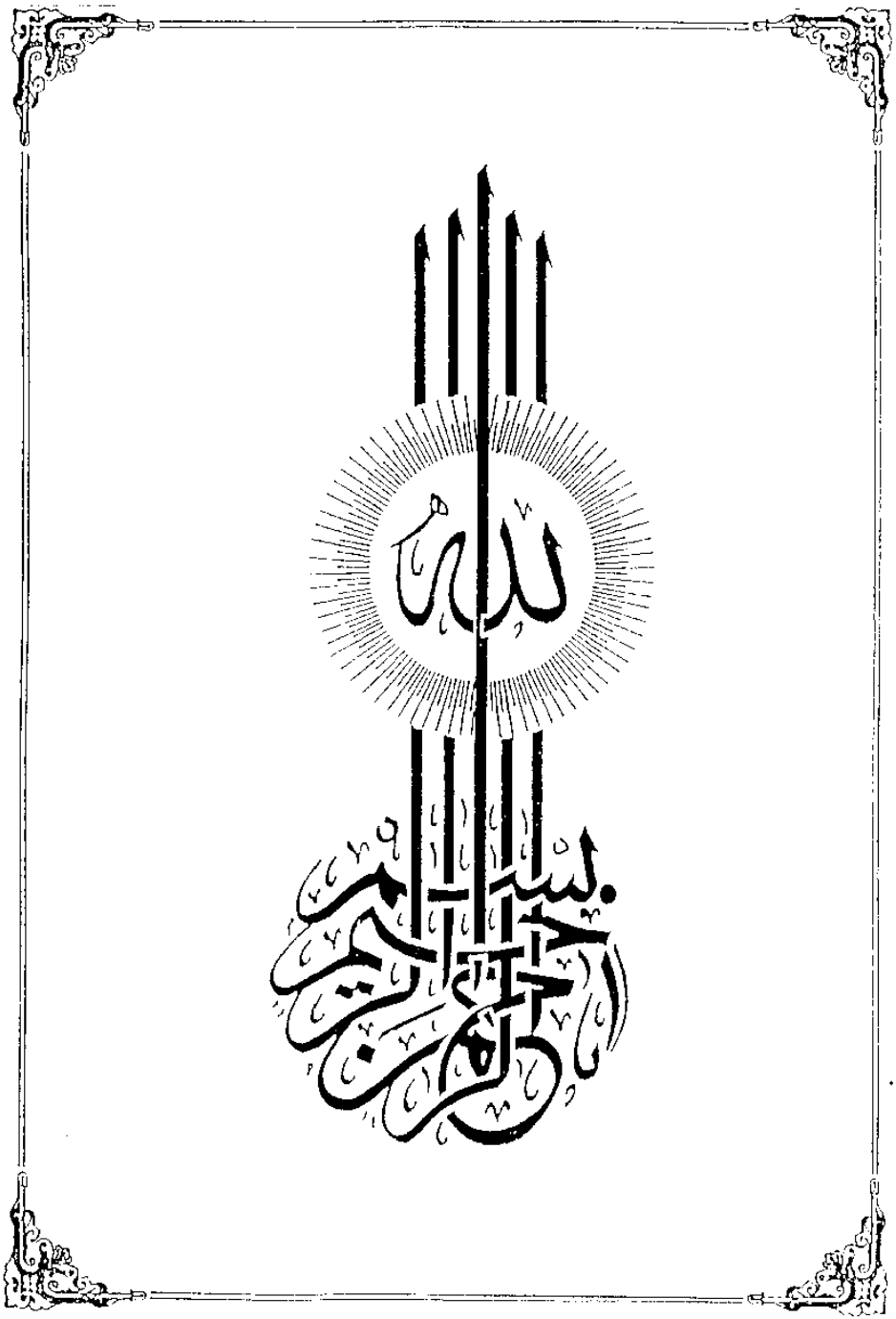
I am deeply grateful to Dr. Ashraf Mahmoud Okba, Lecturer of Internal Medicine, Ain Shams University, for his kind advice, help and supervision.

I wish to express my deepest gratitude to Dr. Mohamed Saad Younis, Lecturer of Parasitology Banha Faculty of Medicine, for his great help.

Special gratitude to Dr. Mohamed El-Azazi, Lecturer of Internal Medicine, Ain Shams University, for his great help and supervision.

I am deeply indebted to my family for their help and encouragement.

Lastly, my particular appreciation and best wishes to all patients and hope for recovery.



Contents

LIST OF ABBREVIATIONS

AIDS	Acquired immune defeciency syndrome
C GCA	C. glycocholate
D.M.	Diabetes mellitus
FBS	Fasting blood sugar
GAD	Glutamic acid decarboxylase
GIT	Gastrointestinal tract
HLA	Human Leucocyte Antigens
ICA	Islet Cells antibodies
IDDM	Insulin-dependent diabetes mellitus
IgA	Immunoglobulin A
IGT	Impaired glucose tolerance
IMMC	Interdigestive migration motor complex
JOD	Juvenile onset diabetes
MOD	Maturity onset diabetes
Nacl	Sodium chloride
NBT	Nitroblue-Tetrazolium Test
NIDDM	Non insulin-dependent diabetes mellitus
PICA	Pancreatic Islet cells antibodies
PPBS	Postprandial blood sugar
PPDs	Standered purified protein derivatives
Tu	Tuberculin unit
Z-N	Ziehl-Neelsen

List of Tables and Figures

INTRODUCTION AND AIM OF THE WORK

Introduction
and
Aim of the Work

Idiopathic diarrhea is a common complication of diabetes mellitus, multiple pathogenic mechanisms have been implicated, autonomic neuropathy and bacterial overgrowth *(Ogbonaya and Arem, 1990)*. For a long time, diabetics have been widely believed to be more susceptible to various types of infections which account for the high mortality rates in these cases in the pre-insulin era and before the advent of antibiotics *(Leonard et al., 1989)*.

In fact, the risk of infections in a poorly controlled diabetics is far more than in a well controlled patients. A leucocytic chemotactic defect has been reported at elevated blood glucose level, also, phagocytic and bactericidal activity is reduced *(Stites and Terr, 1991)*.

The individual immunologic status is a very important factor in determining the susceptibility to infection by cryptosporidia and the severity of it which

is first discovered in an immunocompromised patients *(Meisel et al., 1976).*

Cryptosporidiosis is considered as one of the diarrheal diseases that affect mildly the normal individuals and become more prevalent and more severe in immunocompromised patients whatever the cause *(Nelson et al., 1992).*

It will be of interest to study the incidence and prevalence of cryptosporidiosis in cases of diabetic diarrhea.

Diabetes Mellitus

Defenition and classification:

Diabetes mellitus is a clinical syndrome characterized primirly by chronic hyperglycemia and glucosuria.

It is caused by heterogenous group of disorders, which have in common either defeciency or diminished effectiveness of endogenous insulin resulting in a disturbance of carbohydrate, protein and lipid metabolism.

If the disease is prolonged, it is usually complicated by degenerative changes in the blood vesseles of the retina, Kidney and the nervous system.

The traditional classification of diabetes mellitus is based on the age of onset of the disease namely "early onset or juvenile onset diabetes (JOD)" and "late onset or maturity onset diabetes (MOD)".

JOD has its onset, chiefly in children, adolescents and young adults in which symptoms are severe and the

overall course is aggressive. The other variety occurs chiefly in old persons. It is often has an insidious onset with relatively few or no symptoms and a much greater tendency to obesity.

Another form of diabetes was described resembling maturity onset diabetes in characters, but occur in a younger age called "maturity onset diabetes of the young" (MODY) *(Tattersall and Fajons, 1975).*

The term juvenile and maturity onset are regarded unsatisfactory and misleading. Some old patients may develop diabetes that is insulin dependent, on the other hand. The characters of maturity onset diabetes may be presented in a young patient as previously mentioned.

Genetic and immunological information have led to the need for a revised classification.

The following classification was produced by jerrold 1992:-

1- **Primary diabetes mellitus:-**

Type I: Insulin - dependent (IDDM) or Ketosis prone diabetes it can be further subdivided into:

Type I-A: Transient PICA (Pancreatic islet cell antibodies), no other autoimmune features.

Type I-B: Persistant PICA (*pancreatic* islet cell antibodies) other autoimmune features are present.

Type II: Non insulin-dependant NIDDM

obese 80%

Non obese 20%

2- Secondary diabetes due to :-

A- Pancreatic disease e.g., Pancreatectomy, pancreatic insuffeciency, hemochromatosis.

B- Hormonal Excess counter insulin hormones e.g, Cushing's syndrome , acromegally, pheochromocytoma.

C- Drug induced e.g., thiazide diuretics, steroids, phenytoin,

D- Associated with specific genetic syndrome, e.g., lipodystrophy, myotonic dystrophy, ataxia - Telangectasia.

3- Impaired glucose Tolerance (IGT).

4- Gestational diabetes.

Type I (D.M) (IDDM):

The common characteristics of this form are, sudden clinical onset, severe hyperglycaemia, The easy appearance of Ketoacidosis and severe insulin defeciency. Most of the cases occur in individual aging below 25 years, hence it was formerly termed "juvenile diabetes" *(Cudworth, 1976).*

In epidemiological studies, there is a peak incidence between 11 and 13 years of age and an additional small peak in the third decade *(Cudworth 1981).*

Both subgroup of type I, D.M. have circulating islet cell antibodies, with abnormal immune response and autoimmunity as etiological factors.

Pancreatic islet cell antibodies are detected immediatly after the onset of the disease, but in type IA they are transient. In type IB, Pancreatic islet cell antibodies may be detected long before the onset and may

persist for many years afterwards. Antibodies to other endocrinal tissus are also found in type IB insulin dependent diabetes mellitus *(Bottazzo and donish, 1976).*

IDDM susceptibility is related to the inheretence of specific alleles at HLA class II loci - HLA DR3,4 and DQ2,8 on haplotypes such as HLAA1, B8, DR3 in caucasoids *(Harrison et al., 1993).* The frequencies of DR3 and DR4 were higher in the at-Risk first degree relatives than in the controls, Although the antigen frequency of DR3 was significantly greater in both antibody and T-cell responders than in controls, These were a striking difference in haplotypes.

The frequency of the B8, DR3 haplotype was increased in comparison with controls only *(Harrison et al., 1993).*

As autoimmune disease, insulin-dependent diabetes mellitus is thought to result from T-cell mediated destruction of pancreatic islet beta cells *(Harrison et al., 1990).* Islet reactive T cells have been detected in the peripheral blood of people with clinical IDDM of recent onset and in IDDM patients. Symptom free first degree relatives positive for islet-cell antibodies

(ICA). as well as ICA up to 70% of at risk first degree relatives have circulating antibodies against native or recombinant glutamic acid decarboxylase (GAD) *(Harrison et al., 1993).*

This enzyme, which catalyzes the conversion of glutamic acid to gamma - amino butyric acid is present in high concentrations in brain and pancreatic islets. GAD in pancreatic beta cells is an autoantigen in IDDM.It was found that, high concentration of circulating autoantibodies that precipitate nativeGAD activity were associated with low proliferation of peripheral blood T cells to recombinant GAD., conversely, low concentrations of autoantibody to GAD were associated with high T.cell proliferation to GAD *(Harrison et al., 1993).*

It is postulated that, if GAD is a pathogenetic autoantigen, sensitisation to beta - cell GAD is more likely to lead to IDDM when the immune response deviate towards the expansions of autoreactive T cells rather than towards generation of autoantibodies.

This idea is consistent with evidence that beta cell destruction is mediated by T cell and that high