DETECTION OF SERUM IMMUNE COMPLEXES IN CHILDREN WITH INSULIN-DEPENDANT DIABETES MELLITUS

Thesis
Submitted For The Partial Fulfilment
of Master Degree in Pediatrics

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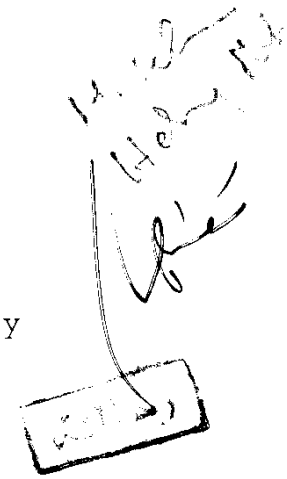

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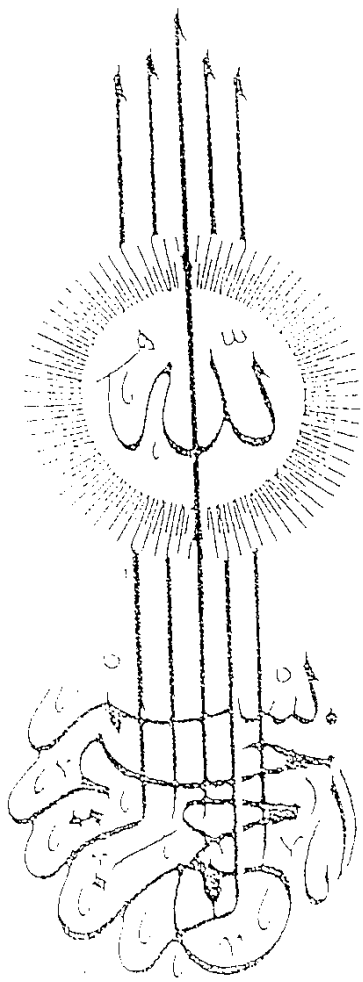

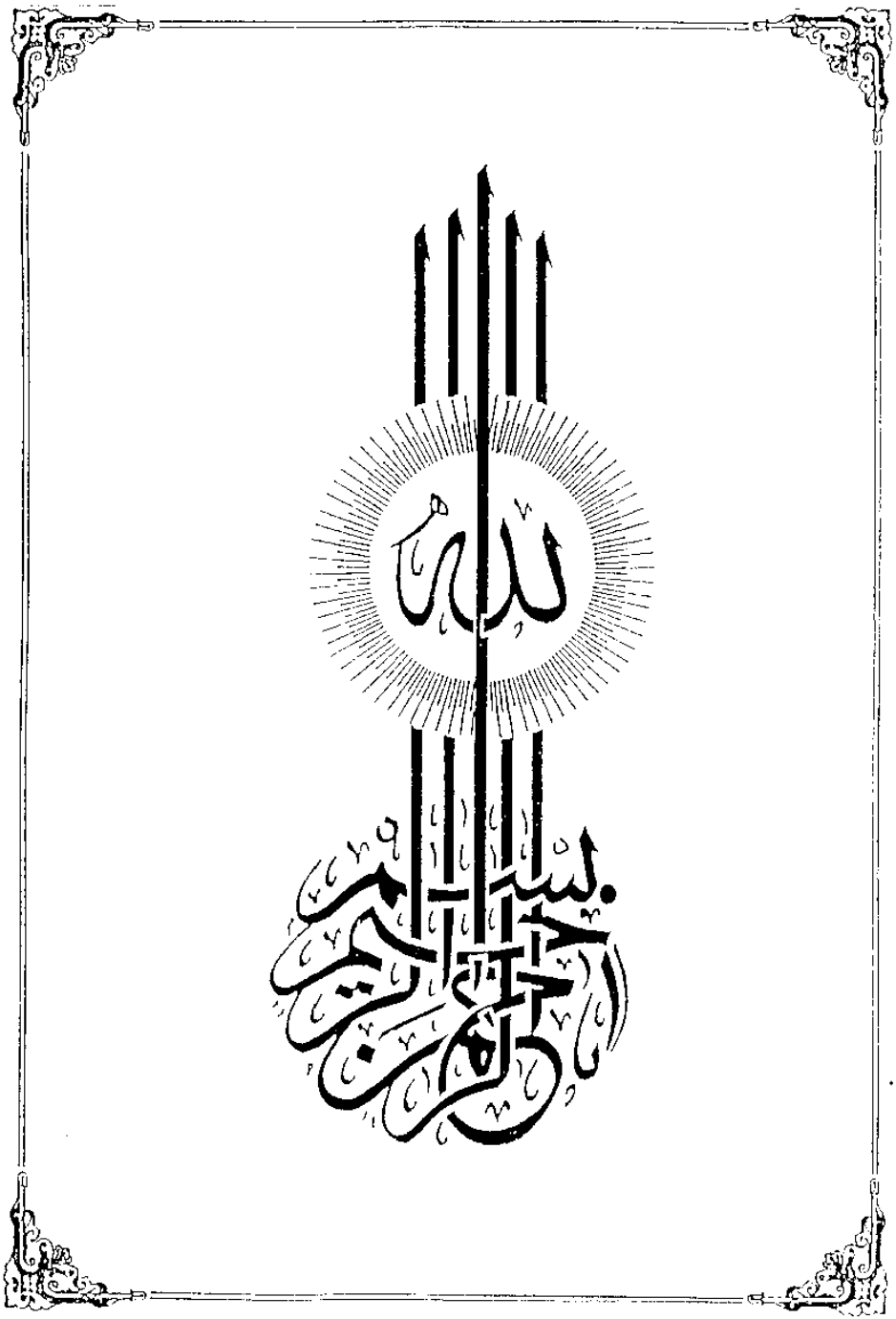

CONTENTS

page

INTRODUCTION AND AIM OF THE WORK 1

REVIEW OF LITERATURE 3

Part I: Diabetes Mellitus 3
Classification and clinical features 4
Diagnosis of IDDM 18
Complications of IDDM 20

Part II: Immune Complexes 22

MATERIAL AND METHODS 30

RESULTS 36

DISCUSSION 53

SUMMARY AND CONCLUSION 58

REFERENCES 60

ARABIC SUMMARY ..... -

ACKNOWLEDGEMENT

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Thanks first to God.

Then I wish to express my deepest gratitude to Dr. Mona Salem, Ass. Prof. of Pediatrics, Ain Shams University. She provided me with the apportunity to work on this research under her guidance of which I'm much proud. She revised every work in this thesis and to her advice, constructive discussion and creticism, I am much obliged.

I am much indebted to the great help offered by Dr. Rasha Khalil, Ass. Prof. of Bacteriology, Ain Shams University. She sincerely helped me, provided much of her time and offered me valuable assistance and sincere help.

INTRODUCTION
AND AIM OF THE WORK

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In 1970, a completely new outlook on the pathogenesis of insulin dependant diabetes mellitus (IDDM) was developed. Clinical studies suggested a relationship between (IDDM) and other organ specific autoimmune diseases (Irvine et al, 1970). It was reported that there was a modification in the cell mediated immune response (Nerup et al., 1973) as well as an association with particular histocompatibility antigens (HLA) (Nerup et al., 1974).

The antigens involved in circulating immune complexes (CICs.) formation may be host cell membrane or other components or exogenous antigens. In the latter situation, complexes may be formed in the circulation with subsequent localisation in vessel wall or perivascular tissues (Di Mario et al., 1980).

Immune components were found in microangiopathic vessels and diabetic like lesions were experimentaly induced by immune mechanisms especially in the renal glomeruli (Andreev et al., 1970).

This stimulated us to do the present study to investigate the sera of insulin-dependant diabetics compared to that in controls to see their possible role in the pathogenesis of

insulin-dependant diabetes mellitus.

REVIEW OF LITERATURE

PART I

DIABETES MELLITUS

REVIEW OF LITERATURE

Diabetes mellitus

Diabetes mellitus is the commonest endocrinal and metabolic disease in childhood (Drash, 1975) and (Tattersal and Fohnston, 1981).

It has been clearly established that diabetes mellitus is genetically and clinically heterogeneous group of disorders that share glucose intolerance in common (Rotter and Rimoin, 1978).

The evidence in favour of this heterogeneity is over-whelming:-

* There are more than 30 distinct mostly rare disorders in which glucose intolerance is a feature.

* Ethnic variability in prevalence and clinical features.

* Genetic heterogeneity in diabetic animal models.

* Clinical variability between thin, ketosis - prone, insulin - dependant diabetes and obese, non ketotic insulin - resistant diabetes.

* Genetic and immunologic studies show that juvenile and

adult onset diabetes are two distinct entities.

* Demonstration that there is a type of mild diabetes in young people which is inherited in an outosomal dominant fashion is clearly different from the classic acute - onset diabetes of juveniles (Fajans et al., 1978 and Rotter et al., 1978).

These collective evidences has been used to classify diabetes mellitus.

Classification and clinical features

Report of the National Commission Diabetes, (1975) put the classification of diabetes mellitus and the clinical characteristics of the two major types, as shown in tables A and B.

With few exceptions, diabetes in children is of the insulin - dependant variety previously called "Juvenile onset diabetes mellitus" (Sperling 1979).

Table A: Classification of Diabetes Mellitus

Traditional Clinical Classification (with Alternate Nomenclature)	NIH Diabetes Data Group Classification
1. Juvenile-onset-type Diabetes(JOD):- a) Ketosis - prone diabetes. b) Juvenile - onset diabetes. c) Severe diabetes. d) Brittle diabetes.	1. Insulin - Dependant Diabetes Mellitus, type I (IDDM).
2. Maturity-onset-type-Diabetes(MOD):- a) Adult-onset diabetes (AOD) b) Ketosis-resistant diabetes c) Mild diabetes d) Obesity-hyperglycemia e) Maturity-onset diabetes f) Stable diabetes.	2. Non-insulin-Dependant Diabetes Mellitus Type II (NIDDM). 1- Non-obese NIDDM. 2- Obese NIDDM.
3. Maturity-onset-type diabetes in the young (MODY) . a) Familial maturity diabetes. b) Maturity-onset diabetes of youth.	3. Gestational diabetes
4. Gestational Diabetes.	4. Diabetes Mellitus and Impaired glucose tolerance associated with other conditions.
5. Secondary diabetes.	5. Diabetes Mellitus secondary to congenital insulin receptor deficiency.
6. Congenital Insulin Resistance with Acanthosis Nigricans.	6. Diabetes Mellitus secondary toinsulin receptor antibody.
7. Acquired Insulin Resistance with Acanthosis Nigricans.	7. Diabetes Mellitus secondary to Familial Autoimmunity .
8. Familial Autoimmune Diabetes.	

Diabetes 28 : 1039 - 1057 / NIH = National Institute of Health

B: Clinical Characteristics of the two major types of diabetes mellitus.

NIH Diabetes Data Group Terminology	Insulin Dependent Diabetes Mellitus (IDDM)	Non-Insulin Dependent Diabetes Mellitus (IDDM)
Alternate Clinical terminology	Juvenile-onset diabetes (JOD) Brittle Diabetes	-Maturity-onset Diabetes (MOD) -Adult onset Diabetes (AOD) -Stable Diabetes.
-Clinical Features :		
-Age of onset	Usually less than 45 years rare in newborn,but increases in frequency at pread-olescence (10-14 years of age).	Usually over 30 years
-Onset	Often rapid	Insidious
-Weight	Non obese	Often obese
-Ketosis	Common	Rare
-Epidemiology :		
Prevalence	0.05 %	2 %
Sex	Sliqht male pre-dominance	Female predominance
Seasonal variation	Present	?
-Pathology :		
Islet mass	Severely reduced	Moderately reduced
Insulinitis at onset (Inflammation in the islet cells).	Present in 50-70 %	?
-Genetics :		
Concordance rate of identical twins.	50 %	90 %
Association with human leukocyte antigens (HLA).	Present	Absent
-Immunology :		
Associated with other endocrinopathies.	Frequent	Infrequent
Anti - islet cell immunity		
Humoral	60-80 % at onset	5-20 %
Cell-mediated	35-50 % at onset	5 %

Clements et al., 1978