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THE FREQUENCY OF THE ANTI GAD ANTIBODY IN A SRI LANKAN DIABETIC POPULATION

by

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DECLARATION BY CANDIDATE

I hereby declare that the work described in this thesis was carried out by me under the supervision of Dr. Sisira H. Siribaddana and any report on this has not been submitted in whole or in part to any university or any other institution for another Degree/Diploma.

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DECLARATION BY SUPERVISOR

I certify that the above statement made by the candidate is true and that this thesis is suitable for submission to the University for the purpose of evaluation.

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Dedicated to my wife Subo, for her love, patience and understanding.

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LIST OF ABBREVIATIONS

ABBOS	Antibodies to Bovine Serum Albumin
ADA	American Diabetes Association
APC	Antigen Presenting Cells
APS	Autoimmune Poly-endocrine Syndrome
BMI	Body Mass Index
CBV	Coxsackie B viruses
CMV	Cytomegalovirus
C-peptide	Connecting peptide
CPH	Carboxy-peptidase H
CVB4	Coxsackie virus B4
DPT	Diabetes Prevention Trial
EBV	Epstein Barr Virus
ELISA	Enzyme Linked Immuno Sorbant Assay
FCPD	Fibro-Calculus Pancreatic Diabetes
GABA	Gamma Amino Butyric Acid
GAD	Glutamic Acid Decarboxylase
GADA	Glutamic Acid Decarboxylase Antibody
GDM	Gestational Diabetes Mellitus
GLUT	Glucose-Transporter
HLA	Human Leukocyte Antigen
HSP65	Heat Shock Protein 65
IA-2	Insulinoma Antigen-2

IA-2A	Insulinoma Associated-2 Antibody
IAA	Insulin Autoantibody
ICA	Islet-cell Antibodies
ICA512/IA-2	Protein tyrosine phosphatase
IDDM	Insulin-Dependent Diabetes Mellitus
IFG	Impaired Fasting Glucose
IFN	Interferon
Ig	Immunoglobulins
IGT	Impaired Glucose Tolerance
IL	Interleukin
INOS	Inducible Nitric Oxide Synthase
IVGTT	Intravenous Glucose Tolerance Test
LADA	Latent Autoimmune Diabetes in Adults
MAP	Mean Arterial Blood Pressure
MHC	Major Histocompatibility Complex
MMDM	Malnutrition Modulated Diabetes Mellitus
MODY	Maturity Onset Diabetes of the Young
MRDM	Malnutrition-related diabetes mellitus
NCCLS	National Committee for Clinical Laboratory Standards
NIBSC	National Institute for Biological Standards and Control
NIDDM	Non-insulin dependent diabetes mellitus
NOD	Non Obese Diabetic
OGTT	Oral Glucose Tolerance Test
OND	Other Neurological Diseases

PDDM	Protein-deficient diabetes mellitus
PERM	Progressive Encephalomyelitis with Rigidity and Myoclonus
PP	Pancreatic Poly peptide
PTP	Protein Tyrosine Phosphatase
RBA	Radio Binding Assay
RIA	Radio Immune Assay
SMS	Stiff-Man Syndrome
T1DM	Type 1 Diabetes Mellitus
T2DM	Type 2 Diabetes Mellitus
Th1	T Helper 1 Cells
Th 2	T Helper 2 Cells
TNF	Tumor Necrosing Factor
TRFIA	Time Resolved Fluoro Immuno Assay
Type1A DM	Type 1 Autoimmune Diabetes Mellitus
Type1B DM	Type 1 Idiopathic Diabetes Mellitus
UKPDS	UK Prospective Diabetes Study
WHO	World Health Organization
WHR	Waist Hip Ratio

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were referred from four centers and 383 (39%) were enrolled in the study. Except the sex and the time since diagnosis, three groups (T1DM=87, T2DM=97 and controls=199) were different in all other factors. Time Resolved Fluro-Immuno Assay (TRFIA) was used to measure GAD antibodies. Among 383 individuals, 50 (13.1%) were GADA positive. The mean and the median GADA values (ng/ml) in T1DM 204.5 and 14.0 and in T2DM 19.2 and 7.7 and in non-diabetic controls were 33.8 and 9.4.

The prevalence of GADA among T1DM individuals were 23.0% (95% CI: 14.16-31.84), T2DM individuals 11.3% (95% CI 4.77-17.23) and control population 9.5% (95% CI 5.46-13.63). The value of GADA in these participants (who were positive for GADA) is significantly different with highest among T1DM and lowest among T2DM. There is no significant difference between gender and GAD positivity in all 3 groups. GADA +ve patients with T2DM were older and diagnosed later than T1DM patients. GADA values decreased with time since diagnosis in both type1 and type 2 diabetics. 4% of variation in GADA values can be due to age in patients with T1DM. Antibodies to GAD are present in 23.0 % of our patients when compared with 70% of patients with T1DM in Europe. High percentage of TIDM patients with positive family history (28%) may indicate masquerading LADA in T1DM group. In our results higher (9.5%) percentage of the healthy controls being GAD positive is intriguing. This may be due to lower sensitivity of the test. In addition, it may be due to higher background autoimmunity in our sample and population.