# Academic Skills in Children with Early-Onset Type 1 Diabetes: Effects of Diabetes-related Risk Factors

*Thesis*

*Submitted for Partial Fulfilment of Master Degree*
*in* ***Pediatrics***

*By*

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*2014*

# Dedication

*This work is dedicated to . . .*

***My beloved father,*** **to whom I owe everything I ever did in my life and will achieve**

***My mother*** **for always being there for me**

***My brother (Sherif) and my sister in law (Dina)*** **for their support**

**Last but not least,** ***my husband (Amr) and my lovely daughter (Nour)*** **for being the light of my life**

# Acknowledgment

First of all, I would like to express my deep gratitude to ALLAH for his care and generosity throughout my life.

*I would like to express my sincere appreciation to* **Prof. Mohamed Abo El-Asrar Mohamed El-Bayoumy,** *Professor of Pediatrics, Ain Shams University for his keen supervision and guidance and his overwhelming support that has been of great help throughout this work.*

*I am very thankful to* **Dr. Nevine Gamal Andrawes,** *Assistant Professor of Pediatrics, Ain Shams University for her great support & effort throughout the whole work.*

*I would also like to express my great thanks to* **Dr./ Menan Abd El-Maksoud Rabie,** *Assistant Professor of Psychiatry, Ain Shams University for the great effort he has done in this work and for helping me through it.*

*I am deeply grateful for the psychologist* **Mr. Abd El Gawad,** *Psychology Specialist, Faculty of Medicine Ain Shams University, for his valuable help in the practical part.*

*Finally my sincere thanks and appreciation to all patients participated in this study and their parents.*

*Mariam El-Sherif*

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# List of Abbreviations

| Abb. | Meaning |
|---|---|
| ADA | American diabetes association |
| Cho | Choline |
| CNS | Central nervous system |
| Cr | Creatine |
| CRP | C-reactive protein |
| DCCT | Diabetes control and complication trial |
| DKA | Diabetic ketoacidosis |
| ECS | Expected correct score |
| EDIC | Epidemiology of diabetes interventions and complications |
| EES | Expected error score |
| FBG | Fasting blood glucose |
| GADA | Glutamic acid decarboxylase |
| Glc | Glucose |
| HbA1C | Glycated hemoglobin |
| HHS | Hyperglycemic hyperosmolar state |
| HLA | Human leukocyte antigen |
| HNF-4 | Hepatocyte nuclear factor |
| IAA | Insulin auto –antibodies |
| ICA | Islet cell cytoplasmic auto- antibodies |
| IDF | International diabetes federation |
| Ins | Myo-inositol |
| KCNJ11 (Kiro 6.2) | Inward-rectifier potassium ion channel gene |
| MHC | Major histocompatibility complex |
| MODY | Maturity onset diabetes of the young |
| MRBG | Mean random blood glucose |
| MRI | Magnetic resonance imaging |
| MRS | Magnetic resonance spectroscopy |
| NAA | N- acetyl aspartate |
| NEFA | Non esterified fatty acids |
| Neuro D1 | Neurogenic differentiation |

# List of Abbreviations (Cont...)

| Abb. | Meaning |
|---|---|
| NGSP | National glycohemoglobin standardization program |
| NKT | Natural killer T cells |
| OCS | Obtained correct score |
| OES | Obtained error score |
| OGTT | Oral glucose tolerance test |
| PIQ | Performance IQ |
| PPG | Post prandial glucose |
| SMBG | Self-monitoring of blood glucose |
| SPET | Single photo emission tomography |
| T1DM | Type 1 diabetes mellitus |
| TAG | Triacylglycerol |
| TDD | Total daily dose |
| Th | T helper cells |
| TIQ | Total IQ |
| VIQ | Verbal IQ |
| WCST | Wisconsin card sorting test |
| WISC | Wechsler intelligence scale |

# Abstract

**Background:** Diabetes Mellitus has a marked effect on brain function and structure in children and adolescents. Cognitive dysfunction should be listed as one of the many complications of diabetes, along with retinopathy, neuropathy, nephropathy, and cardiovascular.

**Objective:** To determine the effect of diabetes –related risk factors on cognitive functions in children with Type 1 Diabetes Mellitus.

**Subjects and Methods:** A total of 50 children and adolescents with T1DM with mean age (11.76%±1.95**)** compared to 25 healthy controls age and sex matched. Patients were subdivided into 2 groups according to their glycated hemoglobin with mean HbA1c8.42±1.89% (group 1:HbA1c more than 7.5%, group 2: HbA1c less than 7.5%).Patients were subjected to full history taking regarding (age of onset, insulin therapy, no. of attacks of hypoglycemia and diabetic keto acidosis).

**Results:** There was a positive correlation between the age of onset of diabetes and cognitive dysfunction, the earlier the age the more cognitive dysfunction (p less than 0.05)**,** significant difference was found between poor glycemic controlled patients and good glycemic controlled patients (p less than 0.05), a correlation was found between patients with history of one or more attacks of DKA and patients with no history of DKA attack (p less than 0.05), no correlation was found between frequency of attacks of hypoglycemia and cognitive functions affection.

**Conclusion:** Patients with T1DM have been found to have cognitive deficits that can be attributed to their disease. Early age onset, poor glycemic control and DKA is an important risk factor.

# 1INTRODUCTION

Type 1 diabetes (T1D) is an autoimmune disease in which a person's pancreas stops producing insulin, a hormone that enables people to get energy from food. It occurs when the body's immune system attacks and destroys the insulin-producing cells in the pancreas, called beta cells, scientists believe that both genetic factors and environmental triggers are involved ***(Canivell and Gomis, 2014).***

An association between early-onset type 1 diabetes mellitus (T1DM)"before the age of 5 years" and cognitive and neural dysfunction has been demonstrated. However, the mechanism underlying deficient neurodevelopment remains unclear. Hypotheses have been proposed concerning the effect of extreme levels of plasma glucose on brain metabolism and neural functioning. The timing of the metabolic insult in a child's development seems to be an important predictor of the outcome ***(Northam et al., 2010, Desrocher et al., 2004).***

Children with an earlier onset of T1DM have lower cognitive and academic skills than those with "after the age of 5 years"T1DM or healthy children ***(Gaudieri, 2008).*** In addition to the early onset of T1DM, several risk factors, in particular severe hypoglycaemia and prolonged hyperglycemia have shown to affect cognitive development ***(Perantie et al., 2008).***

Poor glycaemic control in the 1st year of type 1 diabetes is associated with poorer academic skills indicating the effect of the timing of metabolic aberrations on the cognitive development ***(Hannonen, 2012).***

# Aim of the Work

The study aims to assess the effects of diabetes-related risk factors on the cognitive development of children with an early-onset type 1 diabetes mellitus (T1DM).