

Correlation between glucose, insulin and sulfur containing amino acids levels in N.I.D.D.M

Thesis
Submitted in Partial Fulfillment for
the M.Sc. Degree in Endocrinology

Presented by
Dr. Amr Aly Mahfouze
M.B., B.Ch.

Under Supervision of

Prof. Dr. Soheir M. Gamal El Din
Prof. of Medicine and Endocrinology
Ain Shams University

Dr. Magda Shokry Mohamed
Lecturer of Medicine
Ain Shams University

Prof. Dr. Ibrahim M. A. El-Agouza
Prof. of Physiology
Faculty of Science
Cairo University

1997

5/15-97
A.A

52797



بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

وَقَضَىٰ رَبُّكَ أَلَّا تَعْبُدُوا إِلَّا إِيَّاهُ وَبِالْوَالِدَيْنِ

إِحْسَانًا إِمَّا يَبْلُغَنَّ عِنْدَكَ الْكِبَرَ أَحَدُهُمَا أَوْ

كِلَاهُمَا فَلَا تَقُلْ لَهُمَا أُفٌ وَلَا تُنْهَرَهُمَا وَقُلْ

لَهُمَا قَوْلًا كَرِيمًا *

صَدَقَ اللَّهُ الْعَظِيمُ



To My
Great Father and Mother

ACKNOWLEDGEMENT

At the outset of this work . I would like to acknowledge the efforts of all who have contributed in various ways to the realization of this study .

I would like to express my indebtedness to my supervisor , Dr. Soher Mohamed Gamal EL-Dain , Professor of medicine and Endocrinology, Ain Shams University for suggesting the topic and for supervision during the practical work, and for fruitful discussions during the preparation of the manuscript and final revision of the work at its completion. Her support is greatly appreciated both at the inception and termination of the work.

I also wish to extend my deep thanks to Dr. Magda Shokri, Lecturer of medicine, Ain Shams University for supervising and fruitful discussions during the preparation of the manuscript.

My deepest gratitude and faithful thanks are extended to Dr. Ibrahim Mohamed Ali El Agouza, Professor of Physiology, Zoology, Department , Faculty of science, Cairo University for the time and efforts he spent during the preparation of the laboratory work which measured in Neuroendocrine Research Unit and for supervising in guiding me to the perfect way to accomplish this study.

True thanks to my wife for her effort in offering me the statistical tools used in this study and the sacrifice she offered me during the long hours I spent in preparing this work.

Contents

	Page
Introduction and Aim of the work.	1
I- Sulfur Containing Amino Acids:	3
- Amino acids.	3
- Taurine.	4
- Distribution of taurine.	5
- Physicochemical considerations of taurine.	7
- Metabolism of taurine.	9
- Osmoregulation.	10
- Taurine uptake.	12
- Taurine release.	13
- Calcium modulation.	15
- The protective effects of taurine on kidney and liver.	17
- Role of taurine in modulation of platelet function.	24
- Hypo lipidimic effect of taurine.	25
- Taurine and carbohydrate metabolism.	26
II- Diabetes Mellitus:	31
- Definition.	31
- Classification and etiology.	31
- Type I : Insulin-Dependent.	31
- Aetiology and pathogenesis of I. D. D. M.	32
- Genetics of type I Diabetes.	32
- Enviromental factors.	32
- Autoimmune mechanisms.	33

	Page
- Type II : Non insulin dependent.	33
- Aetiology and pathogenesis of N.I.D.D.M.	34
- Genetic Factors.	34
- Environmental Factors.	36
- Diet.	36
- Obesity.	37
- Non obese N.I.D.D.M	38
- Aging.	38
- Physical activity :-(training & exercise).	39
- Stress.	39
- Insulin Resistance in N.I.D.D.M.	40
- Binding defects.	40
- Post binding defects.	40
- Insulin Secretion in NIDDM.	41
- Secondary Diabetes.	43
- Pancreatic disease.	43
- Drug Toxicity.	44
- Endocrine disorders.	44
- Glycosylated hemoglobin (hemoglobin A _{1c}).	44
III- Material and Methods:	46
- Methods.	46
- Measurement of Creatinine.	47
- Measurement of Urea.	47
- Measurement of GOT and GPT.	48
- Measurement of fasting blood glucose.	49
- Measurement of Insulin.	50
- Measurement of Taurine.	51
- Measurement of (HbA _{1c}).	58

IV- Results.	Page 56
V- Discussion.	68
VI- Summary and Conclusion.	73
VII- References.	75
VIII- Arabic Summary	104

List of Tables

	Page
Table (1) Values of different parameter in healthycontrol subjects.	56
Table (2) Values of different parameter in controlled diabetic patients.	57
Table (3) Values of different parameter in uncontrolled diabetic patients.	58
Table (4) Comparison between different parameters in healthy control and controlled diabetic patients.	59
Table (5) Comparison between different parameters in healthy control and uncontrolled diabetic patients.	59
Table (6) Comparison between different parameters in controlled and uncontrolled diabetic patients.	59
Table (7) Correlation between serum taurine and other measured parameters in healthy subjects.	60
Table (8) Correlation between serum taurine and other measured parameters in controlled diabetic patients.	60
Table (9) Correlation between serum taurine and other measured parameters in uncontrolled diabetic patients.	60

List of Figures

	Page
Fig.(1): Serum level of F.B.G. in different groups.	61
Fig.(2): Serum level of HbA _{1c} in different groups.	62
Fig.(3): Serum level of Insulin in different groups.	63
Fig.(4): Serum level of Taurine in different groups.	64

List of Abbreviations

- AGEs	Advanced Glycosylation End Products
- Anti GAD	Glutamic Acid Decarboxylase
- ATP	Adenosive Tri Phosphate.
- cAMP	3',5' cyclic Monophosphate.
- CCl ₃	Carbon Trichloride.
- CCl ₄	Carbon Tetrachloride.
- D.K.A	Diabetic Keto Acidosis
- D.M	Diabetes Mellitus.
- F.B.G	Fasting blood glucose.
- G.F.R	Glomerular Filtration Rate
- GABA	Gama Amino Butyrate Acid.
- GHb	Glycated hemoglobin.
- GLUT ₄	Glucose Transport Protein.
- H.L.A	Human Leucocytic Antigen
- HbA _{1c}	Hemoglobin A _{1c} .
- HPLC	High performance liquid chromatography.
- I.D.D.M	Insulin Dependent Diabetes Mellitus.

- IM-9 Human Lymphocyte
- LDH Lactate dehydrogenase.
- MDH Malate dehydrogenase.
- MODY Maturity Onset Diabetes of the Young.
- N.I.D.D.M Non Insulin Dependent Diabetes Mellitus.
- PHHI Persistence Hyperinsulinemic Hyperglycemia of Infants.
- Pka Acidic Dissociation Constant.
- RBCs Red Blood Cells.
- S.T.Z Streptozocin.
- SGOT Serum Glutamate oxalo Acetate Transaminase
- SGPT Serum Glutamate oxalo Acetate Pyruvate.
- TGF- β Transforming Growth Factor- β .

**Introduction and
Aim of work**

Introduction and Aim of the work

Sulfur containing amino acids (taurine) that has putative nutritional, osmoregulatory and highly concentrated within a variety of cells especially liver cells (Vadagam et al., 1991).

Plasma level of taurine are regulated by the kidney where the amino acid is reabsorbed in the proximal tubules (Waterfield et al., 1991).

It was proved that taurine has a renal protective effect (Mccoy et al., 1988 and Walker & Shah 1988 and El-Agouza 1994_a).

Hepatic taurine stores are maintained by biosynthesis from sulphur containing amino acids and by uptake via Na^+ and Cl^- dependent system, which is specific for β amino acids (Bucuvalas et al., 1987 and Berkowitz et al., 1994).

It was reported that taurine has a hepatoprotective effect (Guertin et al., 1991 and El-Agouza 1994_b).

It was shown that taurine has hypoglycemic effect by (Kulakous. R. and Joseph Maturo 1984).

All the hypoglycemic effect of taurine were done in the experimental animal.

So, in this work we try to visualize the correlation between serum taurine, glucose, insulin, H_{A1c} levels in control and uncontrolled diabetic.