Hepatic changes in diabetes mellitus and its correlation to the duration of diabetes mellitus and Type of anti-diabetic treatment

Thesis

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بسم الله الرحمن الرحيم

" وقل رب زدنى علما "

صدق الله العظيم

In Sweet Memory of my Late Father

God Bless his Soul

I Hope I made him Proud

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ABSTRACT

This study was conducted on 180 diabetic patients and 20 persons as control group .The patients were divided into: group I 60 patients (NIDDM) on oral anti-diabetic treatment, group II 60 patients (NIDDM) on insulin treatment, group III 60 patients (IDDM) .For all, complete laboratory investigations and abdominal ultrasonography were done. There were increased incidence of fatty liver in group I and II and few cases with elevated liver enzymes. The liver functions and abdominal ultrasonography results of group III were nearly as the normal control group.

Key words: (Liver Disease – Diabetes Mellitus – Diabetic Medications)

CONTENTS

LIST OF ABBREVIATIONS

- ACEI Angiotensin converting enzyme inhibitors
- ADA American Diabetes Association
- ALT Alanine aminotransferase
- AP Alkaline Phosphatase
- AST Aspartate aminotransferase
- BMI Body mass index
- CAD Coronary artery disease
- CVA Cerebrovascular accident
- CVD Cardio-vascular Disease
- DM Diabetes mellitus
- DPP Dipeptidyl peptidase
- EEG Electro-encephalogram
- FDA Food and Drug Administration
- FPG Fasting plasma glucose
- GAD Glutamic acid decarboxylase
- GDM Gestational diabetes mellitus
- GGT Gamma Glutamyl Transferase
- HBA1c Hemoglobin A1c
- HBV Hepatitis B Virus
- HCV Hepatitis C virus
- HDL High density lipoprotein
- HLA Human leukocyte antigen
- HNF Hepatocyte nuclear factor
- ICAS Islet cell autoantibodies
- IDDM Insulin dependent diabetes mellitus

- IPF Insulin promoter factor
- LDL Low density lipoprotein
- LFTs Liver Function Tests
- MODY Maturity onset diabetes of the young
- NAFLD Nonalcoholic fatty liver disease
- NASH Nonalcoholic steatohepatitis
- NDDG National diabetes data group
- NDDK National Institute of Diabetes and Digestive and Kidney Diseases
- NIDDM Non insulin dependent diabetes mellitus
- OGTT Oral glucose tolerance test
- OPTN Organ Procurement and Transplantation Network
- PAI-1 Plasminogen activator inhibitor-1
- PCR Polymerase Cain Reaction
- PPBG Post prandial blood glucose
- SD Standard Deviation
- SMR Standardized mortality ratio
- SRTR Scientific Registry of Transplant Recipients
- TG Triglycerides
- TIA Transient Ischemic Attack
- TNF-α Tumor necrosis factor - α
- TZDs Thiazolidinediones
- UK United Kingdom
- ULN Upper limit of normal
- USA United States of America
- Vs Versus
- WHO World health organization

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INTRODUCTION

Diabetes mellitus "DM" is a metabolic disorder characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both. The chronic hyperglycemia of diabetes is associated with long term damage, dysfunction and failure of various organs especially the eyes, kidneys, nerves, heart and blood vessels ***(American Diabetes Association (ADA), 2008)***.

Over 246 million people live with diabetes across the world and 4.4 million of those people live in Egypt. Egypt is currently in the top 10 countries with the highest number of people with diabetes and will remain so as 7.6 million Egyptians will have the disease by 2025 ***(International Diabetes Federation, 2008)***.

The liver plays a central and crucial role in the regulation of carbohydrate metabolism. Its normal functioning is essential for the maintenance of blood glucose levels and of a continued supply to organs that require a glucose energy source. This central role for the liver in glucose homeostasis offers a clue to the pathogenesis of glucose intolerance in liver diseases but little insight into the mechanisms of liver disease in diabetes mellitus ***(Levinthal and Tavill, 1999).***

In addition to the well known cardiovascular, renal, and ophthalmic complications of diabetes, liver related complications occur commonly and are often under recognized ***(Harrison 2006)***.

Liver disease is one of the leading causes of death in persons with type 2 diabetes. The standardized mortality rate for death from liver disease is greater than that for cardiovascular disease ***(Tolman, 2004).***

Virtually the entire spectrum of liver disease is seen in patients with type 2 diabetes. This includes abnormal liver enzymes, nonalcoholic fatty liver disease (NAFLD), cirrhosis, hepatocellular carcinoma, and acute liver failure. In addition, there is an unexplained association of diabetes with hepatitis C. Finally, the prevalence of diabetes in cirrhosis is 12.3–57%. Thus, patients with diabetes have a high prevalence of liver disease and patients with liver disease have a high prevalence of diabetes ***(Trombetta et al., 2005).***

Chronic mild elevation of transaminases is frequently found in type 2 diabetic patients ***(Lewis et al., 2002).***

Elevation of serum alanine aminotransferase (ALT), while uncommon (0.5%) in apparently normal subjects, is common in patients with type 2 diabetes ***(Trombetta et al., 2005).***

Although mild elevations in liver enzymes are associated with features of the metabolic syndrome, only raised GGT is an independent predictor of the deterioration of glucose tolerance to IGT or diabetes. As GGT signals oxidative stress, the association with diabetes may reflect both hepatic steatosis and enhanced oxidative stress ***(Nannipieri M 2005).***

Hepatic fat accumulation is a well-recognized complication of diabetes with a reported frequency of 40–70%. Type 1 diabetes is not associated with fat accumulation if glycemia is well controlled, but type 2 diabetes may have a 70% correlation regardless of blood glucose control (***Chatila, 1996)***.

The prevalence of NAFLD in diabetes is estimated at 34–74% ***(Tolman et al.2007)*** and, in diabetes with obesity, at virtually 100%. While once considered a benign process, NASH has been found to lead to cirrhosis and, in some cases, to hepatocellular carcinoma ***(Matteoni et al., 1999)***.

Chan et al., 2003, performed a study to evaluate the safety of hypoglycemic drug therapy in producing acute liver failure or serious liver injury in diabetic patients. They concluded that acute liver failure or injury (not clearly attributable to other known causes) occurred on the order of 1 per 10 000 person-year among diabetic patients treated with oral hypoglycemic drugs or insulin.