Liver Diseases in Type I Diabetes Mellitus

Thesis

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List of Abbreviations

Abb.	Full term
ADA	*American Diabetes Association*
APEG	*Australasian Pediatric Endocrine Group*
BE	*Branching enzyme*
BMI	*Body mass index*
CD	*Celiac disease*
cm	*Centimeters*
DBE	*Debranching enzyme*
DCCT	*Diabetes Control and Complications Trial*
DKA	*Diabetic ketoacidosis*
DNs	*Diabetic neuropathies*
G6Pase	*Glucose-6-phos-phatase*
G6Pase	*Glucosio-6-phosphatase*
GCK	*Glucokinase*
GLUT	*Glucose transporter*
GP	*Glycogen phosphorylase*
GS	*Glycogen synthase*
GSK3	*Glycogen synthase kinase 3*
HAAF	*Hypoglycemia-associated autonomic failure*
HCC	*Hepatocellular carcinoma*
HG	*Hepatic glycogenosis*
ICR	*Insulin to carbohydrate ratio*
IQR	*Inter quartile range*
IR	*Insulin receptor*
IRS	*Insulin receptor substrate*
ISPAD	*International Society for Pediatric and Adolescent Diabetes*
Kg	*Kilograms*
KPa	*Kilopascal*
MODY	*Maturity-onset diabetes of the young*
MR	*Magnetic resonance*

List of Abbreviations Cont...

Abb.	Full term
NAFLD	*Non-alcoholic fatty liver disease*
NASH	*Non-alcoholic steatohepatitis*
NGSP	*National Glycohemoglobin Standardization Program*
PAS	*Periodic acid-Schiff-stained*
PDK1/2	*3-phosphoinositide-dependent protein kinase 1 and 2*
PEPCK	*Phosphoenolpyruvate carboxykinase*
PGM	*Phosphoglucomutase*
PI3K	*Phosphotidylinositide-3-kinase*
PIP2	*Phosphatidylinositol (3,4)-bispho-sphate*
PIP3	*Phosphatidylinositol (3,4,5)-trisphosphate*
PKB/Akt	*Protein kinase B*
PPi	*Pyrophosphate*
PTMs	*Post-translational modifications*
PTPN2	*Protein tyrosine phosphatase non-receptor type 22*
SPSS	*Statistical Package for Social Science*
T1D	*Type 1 diabetes*
T1DM	*Type 1 diabetes mellitus*
UDP	*Uridinediphosphate*
UDPGPP	*UDP-glucosepy-rophosphorylase*
UTP	*Uridine triphosphate*

INTRODUCTION

Diabetes mellitus is a group of metabolic diseases characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Metabolic abnormalities in carbohydrates, lipids, and proteins result from the importance of insulin as an anabolic hormone ***(Kharroubi and Darwish, 2015).***

A complex interaction of genetic and environmental factors can trigger the immune-mediated mechanism responsible for type 1 diabetes mellitus (T1DM) establishment. Environmental factors may initiate and possibly sustain, accelerate, or retard damage to β-cells ***(Bergamin and Dib, 2015).***

Hepatic glycogenosis (HG) is characterized by excessive glycogen accumulation in hepatocytes and represents a hepatic complication of diabetes that particularly occurs in patients with longstanding poorly controlled type 1 diabetes (T1DM). HG has been reported to be a very rare disease, although it is believed to be extremely underdiagnosed because it is not possible to distinguish it from non-alcoholic fatty liver disease (NAFLD) unless a liver biopsy is performed ***(Julián et al., 2015).***

The imaging study (ultrasonography and/or radiological examinations) gives information about the liver alterations (hepatomegaly), but the diagnosis needs to be confirmed by the liver biopsy ***(Giordano et al., 2014).***

Glycogenic hepatopathy (GH) is an under-recognised complication of type 1 diabetes mellitus (T1DM) not controlled to target resulting in hepatomegaly and elevated liver transaminases ***(Irani et al., 2015).***

Fibroscan is anon invasive and not painful technique used in measurement of liver stiffness. Fibroscan may included in management of HCV ***(Chou and Wasson, 2013).***

AIM OF THE WORK

The aim of this study is to determine liver diseases in children and adolescents with type1 diabetes mellitus by detection of elevated liver transminases and confirmed by fibroscan and ultrasound.

Chapter 1

TYPE 1 DIABETES IN CHILDREN

Diabetes mellitus is a common metabolic disorder that is caused by a deficit in the production of (type 1) or response to (type 2) insulin. Diabetes mellitus is characterized by a state of chronic hyperglycemia and such symptoms as weight loss, thirst, polyuria, and blurred *vision* ***(Stolf et al., 2017).***

In most instances, T1DM represent as an immune, if not autoimmune-mediated disorder where patients usually show features of an immunological basis to disease pathogenesis (e.g. autoantibodies or genetic associations with genes governing immune responses) ***(Eisenbarth, 2007).***

Nevertheless, not all patients with T1DM have these characteristics. This variation leads to emergence of the proposed classifications of type 1A (autoimmune) diabetes, for the 70-90% of patients with type 1 disease that have immunological, self-reactive autoantibodies, and type 1B (idiopathic) diabetes, which describes other patients with no evidence of specific pathogenesis ***(Gianani et al., 2010).***

A subset of individuals within this latter group have monogenic forms of diabetes, such as maturity onset diabetes of the young (MODY) ***(Hattersley et al., 2009)***. Despite knowledge gains that could allow for adopting this new set of

terminologies for subgrouping cases of type 1 diabetes, the terms type 1A and type 1B diabetes are not commonly used ***(Dabelea et al., 2007).***

Diabetes can be classified into the following general categories:

1. Type 1 diabetes (due to autoimmune b-cell destruction, usually leading to absolute insulin deficiency).
2. Type 2 diabetes (due to a progressive loss of b-cell insulin secretion frequently on the background of insulin resistance).
3. Gestational diabetes mellitus (GDM) (diabetes diagnosed in the second or third trimester of pregnancy that was not clearly overt diabetes prior to gestation).
4. Specific types of diabetes due to other causes, e.g., monogenic diabetes syndromes (such as neonatal diabetes and maturity-onset diabetes of the young [MODY]), diseases of the exocrine pancreas (such as cystic fibrosis), and drug- or chemical-induced diabetes (such as with glucocorticoid use, in the treatment of HIV/AIDS, or after organ transplantation).

(American Diabetes Association, 2017)