Evaluation of Insulin Resistance in Hepatitis C Infected Thalassemia Children and Survivors of Childhood Malignancy

Thesis
Submitted For Partial Fulfillment of Master Degree in
Pediatrics

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M.B.B., Ch (2007)

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2015

بسم الله الرحمن الرحيم

وقُلِ اعْمَلُوا فَسَيَرَى اللَّهُ عَمَلَكُمْ
ورَسُولُهُ والْمُؤْمِنُونَ

صدق الله العظيم

سورة التوبة آية (١٠٥)

*First, thanks are all due to **Allah** for Blessing this work until it has reached its end, as a part of his generous help throughout our life.*

*I wish to express my deepest sincere gratitude to **Prof Dr. Manal Hamdy EL-Sayed**, Professor of pediatrics, faculty of medicine, Ain shams university, for her kind supervision, great support and encouragement, also for the generous and numerous facilities she had offered all through this work. It has been a great honor to work under her supervision.*

*I am all appreciative for the kind help offered to me by **Dr. Dalia Nabil Toaima**, Lecturer of Pediatrics, faculty of medicine, Ain shams university,. Her scientific guidance, interest, valuable criticism and comments were helpful throughout the course of this work.*

*My deepest thanks to **Dr. Noha Refaat Mohamed**, Lecturer of Clinical and chemical Pathology, faculty of medicine, Ain shams university, for her valuable guidance, serious and decisive comments, continuous support and her meticulous supervision.*

*My deepest thanks to **Dr. Amira Mohsen Abd-Elhamed**, researcher at the community medicine department at national research center for her valuable guidance and helping us doing statistical analysis of this study*

I want to express my deepest gratitude and my great thanks to my dear father who died before I complete this work and I wish if he was present now with me

Finally I would like to thank all the patients and all the volunteers included in this work for their share to complete this work.

Amira Elsayed Abd Elaziz Abd Elgawad

List of Contents

List of Abbreviations

ALP	Alkaline phosphatase
ALT	Alanine transaminase
AST	Aspartate transaminase
BMI	Body mass index
β-TM	B thalassemia major
CHC	Chronic hepatitis C
CIGMA	Continuous infusion of glucose with model assessment
CKD	Chronic kidney disease
CTLs	Cytotoxic T lymphocytes
DM	Diabetes mellitus
EIA-2	Enzyme immunoassay
FFAs	Free fatty acids
GBD region	Global burden of disease regions
GLP-1	Glucagon-like peptide-1
HBs Ag	Hepatitis B surface antigen
HBV–DNA	Hepatitis B virus deoxynucliec acid
HCC	Hepatocellular carcinoma
HCV	Hepatitis C Virus
HCV-Ab	Hepatitis c virus antibody
HCW	Healthcare worker
HD	Hemodialysis
HDL	High density lipoprotein
Hg	Haemoglobin
HIV	Human immunodeficiency virus
HOMA	Homeostasis model assessment
HOMA IR	Homeostasis model assessment insulin resistance
IDU	Injection Drug Use
IGF	Insulin like growth factor

List of Abbreviations (Cont.)

INF α	Interferon α
IR	Insulin Resistance
IRS	Insulin receptor substrate 1
ISDR	Interferon sensitivity determining region
ITT	Insulin tolerance test
IVGTT	Intravenous glucose tolerance test
LDIGIT	Low-dose insulin and glucose infusion test
LDL	Low density lipoprotein
MC	Mixed cryoglobulinemia
MHC	Major histocomptability complex
NCEP	National Cholesterol Education Program
NGT	Normal glucose tolerance
OGTT	Oral glucose tolerance test
PCR	Polymerase chain reaction
PCT	Porphyria cutanea tarda
PT	Prothrombin time
QUICKI	Quantitative insulin sensitivity check index
RA	Rheumatoid arthritis
RIBA	Recombinant immunoblot assay
RNA	Ribonucleic acid
SR-BI	Human scavenger receptor class B1
SS	Sjogren's syndrome
TIBC	Total iron binding capacity
TLC	Total leucocytic count
TMA	Transcription Mediated Amplification
TS	Transferrin saturation
WBC	White blood cell
WHO	World Health Organization

List of Figures

List of Tables

Introduction

Acute HCV infection is rarely recognized in children outside of special circumstances such as a known exposure from an HCV-infected mother or after blood transfusion **(Maureen, 2002).** The risk of acquiring HCV infection as a result of transfusion was about 10**% (Minola et al., 2002)**.

Repeated blood transfusion in thalassemia patients is necessary for their survival; however, such transfusions increase their exposure not only to HCV but also to other blood-borne viruses **(Al-Sheyyab et al., 2001)**. HCV infection is the leading cause of post-transfusion hepatitis worldwide **(Al Hawsawi, 2000)**. Pediatric cancer patients frequently require blood and blood products during therapy; thus, those who were treated before the current HCV blood donor screening methods were initiated in 1992 have an elevated risk of transfusion-acquired HCV. As in the general population, chronic HCV infection in pediatric cancer survivors is associated with liver fibrosis, cirrhosis, hepatocellular carcinoma, extrahepatic manifestations, and impaired quality of life **(Davis et al., 2003).**

There appears to be worldwide geographic variation in the prevalence of HCV infection in children. Studies in the early 1990s (which reflected populations of children who could have been exposed to contaminated blood products) reported prevalence rates ranging from 0 %in Japan and Taiwan **(Tanaka et al., 1992 and Lee et al., 1991)** 4%in Italy **(Gessoni and Manoni, 1993)**. In the United States, antibodies to HCV are present in approximately 0.2 %of children aged 6 to 12 and in 0.4 %of those aged 12 to 19 **(Alter et al., 1999; Jhaveri et al., 2011 and Armstrong et al., 2006).**

Prevalence rates in Egypt were low in the 1990s among children without a history of exposure to blood

products **(Khalifa et al., 1993)** but a more recent series reported HCV rates of 2% **(El_Raziky et al., 2007).**

In an Egyptian study conducted among rural school children reported an average prevalence of about 7% **(Abd El_wahab et al., 1994)** while the average prevalence in children attending outpatient clinics was found to be approximately 4**% (Khalifa et al., 1993).**

High HCV prevalence rates were observed with averages of about 42% among multi-transfused children and about 58% among children with thalassemia **(Mansour et al., 2012).** HCV prevalence among children with leukemia was 19.0**% (Meri et al., 2001).** HCV prevalence among patients with pediatric malignancies who had just ended chemotherapy was 39.6**%(Mostafa et al., 2003).**

It is well documented that HCV infection in children is clinically asymptomatic **(Milner et al., 2010)**. Histological findings are usually mild and the risk of severe complications is low. Nevertheless, despite the favorable prognosis during the first and second decades of life, approximately 4% to 6% of children have evidence of advanced liver fibrosis or cirrhosis **(Guido et al., 2003; Goodman et al., 2008).**

Since the identification of hepatitis C virus (HCV) in the late 1980s, chronic HCV infection has emerged as a complex multifaceted disease with manifestations extending beyond the liver. As such, hepatic steatosis, insulin resistance (IR), and type II diabetes have been observed to occur more frequently in association with HCV infection than other chronic inflammatory liver disease **(Goodman et al., 2008).** Several studies evaluating IR in patients with chronic HCV infection have found that the development of IR can occur early in the course of the disease **(Fartoux et al., 2005).**

This effect appears to be independent of body weight, stage of liver disease, and presence or absence of overt diabetes **(Shintani et al., 2004; Petit et al., 2001).** Hepatitis C makes people three to four times more likely to develop type 2 diabetes and insulin resistance **(Milner et al., 2010).**

This study will assess the association between insulin resistance and hepatitis C in children with thalassemia and the survivors of childhood malignancy.