بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الإلكتروني والميكروفيلم

جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات

يجب أن

تحفظ هذه الأقراص المدمجة بعيدا عن الغبار

MONA MAGHRABY

Evaluation of Serum Markers of Iron Metabolism in Patients with chronic Liver Disease

A Thesis

Submitted for partial fulfillment of Master degree in Pediatrics

By

Eman Ali Hassan Senosy
M.B.B.Ch, Ain Shams University (2012)

Under Supervision of

Prof. Dr. Zainab Anwar El Qabany
Professor of Pediatrics
Faculty of Medicine, Ain Shams University

Dr. Asmaa Wafeeq Abdel Aziz
Lecturer of Pediatrics
Faculty of Medicine, Ain Shams University

Dr. Dina Aly Mohamed
Assistant Professor of Clinical Pathology
Faculty of Medicine, Ain Shams University

Faculty of Medicine
Ain Shams University
2021

بسم الله الرحمن الرحيم

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم الحكيم

صدق الله العظيم

سورة البقرة الآية: ٣٢

Acknowledgments

First and foremost, I feel always indebted to **Allah**, *the Most Beneficent and Merciful who gave me the strength to accomplish this work.*

My deepest gratitude to **Prof. Dr. Zainab Anwar El Qabany,** *Professor of Pediatrics, Faculty of Medicine, Ain Shams University, for her valuable guidance and expert supervision, in addition to her great deal of support and encouragement. I really have the honor to complete this work under her supervision.*

I would like to express my great and deep appreciation and thanks to **Dr. Asmaa Wafeeq Abdel Aziz,** *Lecturer of Pediatrics, Faculty of Medicine, Ain Shams University, for her meticulous supervision, and her patience in reviewing and correcting this work. Also, for guiding me throughout this work and for granting me much of her time. I greatly appreciate her efforts.*

I Cant' forget to thank with all apppreciation **Dr. Dina Aly Mohamed,** *Assistant Professor of Clinical Pathology, Faculty of Medicine, Ain Shams University, for the efforts and time she has devoted to accomplish this work.*

Special thanks to my **Parents,** *my* **Husband** *and all my* **Family** *members for their continuous encouragement, enduring me and standing by me.*

Eman Ali Hassan Senosy

List of Contents

List of Abbreviations

Abbr.	Full-term
ABCB11	**:** Adenosine triphosphate binding cassette, subfamily B, member 11
ABCB4	**:** Adenosine triphosphate binding cassette, **s**ubfamily B, member 4
ABCC2	**:** ATP-binding cassette, subfamily C, member 2
AGS	**:** Alagille Syndrome
AIH	**:** Autoimmune Hepatitis
ALA	**:** Aminolevulinic acid
ATP8B1	**:** Adenosine triphosphatase, type 8B, member 1
BCS	**:** Budd-Chiari syndrome
BMP	**:** Bone morphogenetic protein
CF	**:** Cystic Fibrosis
CFTR	**:** Cystic fibrosis transmembrane conductance regulator
CHF	**:** Congenital hepatic fibrosis
CLD	**:** Chronic liver diseases
CMV	**:** Cytomegalovirus infection
CN	**:** Crigler-Najjar syndrome
CPK	**:** Creatinine phsophokinase
DJS	**:** Dubin Johnson syndrome
DMT1	**:** Divalent metal transporter 1
DNA	**:** Deoxyribonucleic acid
EBV	**:** Epstein bar virus
ERCP	**:** Endoscopic retrograde cholangiopancreatography

ESR : Erythrocyte sedimentation rate
Fe2+ : Divalent ferrous
Fe3+ : Trivalent ferric
FPN : Ferroprotein
Fpn1 : Ferroportin-1
GGT : Gamma glutamyl transpeptidases
GSD : Glycogen Storage Diseases
HAMP : Hepcidin Antimicrobial Peptide
HBV : Hepatitis B Virus
HCV : Hepatitis C Virus
HHC : Hereditary hemochromatosis
IBS : Inspisated Bile Syndrome
IgG : Immunoglobulin G
IL-6 : Interleukin-6
IQR : Interquartile range
IREs : Iron-responsive elements
IRP : Iron regulatory proteins
mRNAs : Messenger ribonucleic acids
MRP2 : Multidrug resistance protein 2
NPC : Niemann–Pick disease type C
NTBI : Non-transferrin bound iron
ORCH : Toxoplasma, rubella, cytomegalovirus, herpes simplex
PBC : Primary biliary cirrhosis
PC : Personal computer
PCR : Polymerase chain reaction
PFIC : Progressive familial intrahepatic cholestases

PKD : Polycystic kidney disease

PSC : Primary sclerosing cholangitis

RES : Reteiclo endothelial system

SD : Standard deviation

SNHL : Sensorineural hearing loss

SPSS : Statistical package for social science

STAT : Signal transducers and activators of transcription

TBI : Transferrin bound iron

Tf : Transferrin

TfR : Transferrin receptors

TIBC : Total iron-binding capacity

TORCH : Toxoplasmosis, Rubella, Cytomegalovirus, Herpes simplex virus

UGT1A1 : UDP-glucuronosyl transferase 1 family, polypeptide A1

WD : Wilson's Disease

List of Tables

List of Figures

Introduction

Iron is essential for most living organisms. In an unbound state, however, it is highly reactive and leads to oxidative stress ***(Ganz, 2013)*** Thus, iron is coupled to transferrin in serum, whereas it is stored in a ferritin-bound form in tissue ***(Ganz, 2013 & Drakesmith, Prentice, 2012).*** Small amounts of ferritin are load. Circulating iron constitutes a small, but highly dynamic iron transit compartment that becomes rapidly altered in disease states ***(Ganz, 2012 &. Gkouvatsos et al., 2012)*** and increased serum iron load leads to emergence of the highly reactive non-transferrin bound iron (NTBI) ***(Brissot et al., 2012 & Koskenkorva-Frank et al., 2013).***

The liver is a critical controller of iron metabolism as it represents a large iron storage compartment and a major producer of ferritin, transferrin and hepcidin ***(Pietrangelo, 2015 & Meynard et al., 2014).*** In chronic liver disease, low concentrations of hepcidin, which blocks the absorption of iron from the intestine and the release of iron from macrophages**,** ***(Ganz, 2012 & Pietrangelo, 2015)*** contribute to parenchymal iron overload, whereas increased hepcidin concentrations, as observed during chronic inflammation, lead to the sequestration of iron within macrophages thereby promoting anaemia ***(Pietrangelo, 2015 & Weiss, 2015).***

As a negative acute phase protein, transferrin is down regulated during episodes of acute inflammation and in advanced liver disease ***(Ritchie et al., 1999 & Potter et al., 1985)***, whereas the acute phase protein ferritin also serves as a surrogate of hepatocellular damage ***(Bhagat et al., 2000).*** In recent years, there accumulated a lot of new data, some of them contradictory, about the clinical significance of serum parameters of iron metabolism as surrogate markers of siderosis and severity of liver disease ***(Weiss, 2015 & Potter et al., 1985).*** There remain open questions regarding the clinical significance of serum parameters of iron metabolism and hepcidin in various chronic liver diseases and the role of some genetic factors and environmental factors for organic liver damage during overload syndrome iron ***(Potter BJ, Chapman RW, Nunes, 1985).***

Aim of the Work

- To describe the parameters of iron metabolism in patients with chronic liver disease

- To measure the correlation between serum parameters of iron metabolism and severity of chronic liver disease.