



شبكة المعلومات الجامعية  
التوثيق الإلكتروني والميكروفيلم

# بسم الله الرحمن الرحيم



**MONA MAGHRABY**



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# شبكة المعلومات الجامعية التوثيق الإلكتروني والميكروفيلم



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# جامعة عين شمس

## التوثيق الإلكتروني والميكروفيلم

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### يجب أن

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**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  
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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

لسبب أنك لا تعلم لنا  
إلا ما علمتنا إنك أنت  
العليم العظيم

صدقة الله العظيم

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## List of Abbreviations

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



<b>ESR</b>	: Erythrocyte sedimentation rate
<b>Fe<sup>2+</sup></b>	: Divalent ferrous
<b>Fe<sup>3+</sup></b>	: Trivalent ferric
<b>FPN</b>	: Ferroprotein
<b>Fpn1</b>	: Ferroportin-1
<b>GGT</b>	: Gamma glutamyl transpeptidases
<b>GSD</b>	: Glycogen Storage Diseases
<b>HAMP</b>	: Hepcidin Antimicrobial Peptide
<b>HBV</b>	: Hepatitis B Virus
<b>HCV</b>	: Hepatitis C Virus
<b>HHC</b>	: Hereditary hemochromatosis
<b>IBS</b>	: Inspisated Bile Syndrome
<b>IgG</b>	: Immunoglobulin G
<b>IL-6</b>	: Interleukin-6
<b>IQR</b>	: Interquartile range
<b>IREs</b>	: Iron-responsive elements
<b>IRP</b>	: Iron regulatory proteins
<b>mRNAs</b>	: Messenger ribonucleic acids
<b>MRP2</b>	: Multidrug resistance protein 2
<b>NPC</b>	: Niemann–Pick disease type C
<b>NTBI</b>	: Non-transferrin bound iron
<b>ORCH</b>	: Toxoplasma, rubella, cytomegalovirus, herpes simplex
<b>PBC</b>	: Primary biliary cirrhosis
<b>PC</b>	: Personal computer
<b>PCR</b>	: Polymerase chain reaction
<b>PFIC</b>	: Progressive familial intrahepatic cholestases

<b>PKD</b>	: Polycystic kidney disease
<b>PSC</b>	: Primary sclerosing cholangitis
<b>RES</b>	: Reteiclo endothelial system
<b>SD</b>	: Standard deviation
<b>SNHL</b>	: Sensorineural hearing loss
<b>SPSS</b>	: Statistical package for social science
<b>STAT</b>	: Signal transducers and activators of transcription
<b>TBI</b>	: Transferrin bound iron
<b>Tf</b>	: Transferrin
<b>TfR</b>	: Transferrin receptors
<b>TIBC</b>	: Total iron-binding capacity
<b>TORCH</b>	: Toxoplasmosis, Rubella, Cytomegalovirus, Herpes simplex virus
<b>UGT1A1</b>	: UDP-glucuronosyl transferase 1 family, polypeptide A1
<b>WD</b>	: Wilson's Disease

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# Introduction

**I**ron 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.