



بسم الله الرحمن الرحيم

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Immunophenotypic Evaluation of Circulating Monocyte Subsets in Beta Thalassemia Major Patients

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

﴿وَأَنْ لِّنَّاسٍ لِلْإِنْسَانِ إِلَّا مَا سَعَى

○ وَأَنْ سَعِيَهُ سَوْفَ يُرَى ○

ثُمَّ يُجْزَاهُ الْجَزَاءُ الْأَوْفَى﴾

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List of Abbreviations

Abb.	Full term
<i>μL</i>	<i>Microliter</i>
<i>Act R</i>	<i>Activin Receptor</i>
<i>Allo-HSCT</i>	<i>Allogenic Hematopoietic Stem Cell Transplantation</i>
<i>ASO</i>	<i>Allele-Specific Oligomer</i>
<i>ATP</i>	<i>Adenosine triphosphate</i>
<i>B-TI</i>	<i>B-Thalassemia Intermedia</i>
<i>B-TM</i>	<i>B-Thalassemia Major</i>
<i>C3/C4</i>	<i>Complement 3/4</i>
<i>CBC</i>	<i>Complete Blood Count</i>
<i>CCL2</i>	<i>Chemokine Ligand 2</i>
<i>CCR2</i>	<i>Chemokine Receptor 2</i>
<i>CCR3</i>	<i>Chemokine Receptor 3</i>
<i>CD</i>	<i>Cluster of Differentiation</i>
<i>CE</i>	<i>Capillary Zone Electrophoresis</i>
<i>CMP</i>	<i>Common Myeloid Progenitor</i>
<i>CO</i>	<i>Carbon monoxide</i>
<i>CRP</i>	<i>C-Reactive Protein</i>
<i>CX3CR1</i>	<i>C-X3-C Motif Chemokine Receptor 1</i>
<i>DAMPS</i>	<i>Damage Associated Molecular Patterns</i>
<i>DCs</i>	<i>Dendritic Cells</i>
<i>DFO</i>	<i>Deferoxamine</i>
<i>DFP</i>	<i>Deferiprone</i>
<i>DFX</i>	<i>Deferasirox</i>
<i>DMT1</i>	<i>Divalent Metal Transporter 1</i>
<i>DNA</i>	<i>Deoxyribonucleic Acid</i>
<i>DPG</i>	<i>Diphosphoglycerate</i>
<i>EPO</i>	<i>Erythropoietin</i>
<i>FITC</i>	<i>Fluoresceine Isothiocyanate</i>

List of Abbreviations (cont...)

Abb.	Full term
<i>FPN</i>	<i>Ferroportin</i>
<i>FSC-A</i>	<i>Forward Scattering Areas</i>
<i>FSC-W</i>	<i>Forward Scatter Width</i>
<i>GDFs</i>	<i>Growth Differentiation Factors</i>
<i>GFR</i>	<i>Glomerular Filtration Rate</i>
<i>Hb F</i>	<i>Fetal Hemoglobin</i>
<i>Hb</i>	<i>Hemoglobin</i>
<i>HBV</i>	<i>Hepatitis B Virus</i>
<i>HCV</i>	<i>Hepatitis C Virus</i>
<i>HH</i>	<i>Hereditary Hemochromatosis</i>
<i>HIV</i>	<i>Human Immunodeficiency Virus</i>
<i>HLA</i>	<i>Human Leucocytic Antigen</i>
<i>HO-1</i>	<i>Heme oxygenase -1</i>
<i>HPLC</i>	<i>High Performance Liquid Chromatography</i>
<i>HS</i>	<i>Hyperhemolysis Syndrome</i>
<i>HSCs</i>	<i>Hematopoietic Stem Cells</i>
<i>ICAM-1</i>	<i>Intercellular Adhesion Molecule-1</i>
<i>ICT</i>	<i>Iron Chelation Therapy</i>
<i>IE</i>	<i>Ineffective Erythropoiesis</i>
<i>IL</i>	<i>Interleukin</i>
<i>IO</i>	<i>Iron Overload</i>
<i>IQR</i>	<i>Interquartile Range</i>
<i>Leu-CAM</i>	<i>Leucocyte Cellular Adhesion Molecule</i>
<i>LFA-1</i>	<i>Lymphocyte Functional Antigen-1</i>
<i>LIP</i>	<i>Labile Iron Pool</i>
<i>LPI</i>	<i>Labile Plasma Iron</i>
<i>LPS</i>	<i>Lipopolysaccharides</i>
<i>Mc Ab</i>	<i>Monoclonal Antibodies</i>

List of Abbreviations (cont...)

Abb.	Full term
<i>MCH</i>	<i>Mean Corpuscular Hemoglobin</i>
<i>MCSF</i>	<i>Macrophage Colony Stimulating Factor</i>
<i>MCV</i>	<i>Mean Corpuscular Volume</i>
<i>MHC</i>	<i>Major Histocompatibility Complex</i>
<i>ml</i>	<i>Milliliter</i>
<i>mo DCs</i>	<i>Monocyte Derived Dendritic Cells</i>
<i>mo MQs</i>	<i>Monocyte Derived Macrophages</i>
<i>MQs</i>	<i>Macrophages</i>
<i>MRI</i>	<i>Magnetic Resonance Imaging</i>
<i>Ng</i>	<i>Nanogram</i>
<i>NK</i>	<i>Natural killer</i>
<i>NO</i>	<i>Nitric Oxide</i>
<i>NTBI</i>	<i>Non Transferrin Bound Iron</i>
<i>NTDT</i>	<i>Non transfusion Dependent Thalassemia</i>
<i>PAMPS</i>	<i>Pathogen Associated Molecular Patterns</i>
<i>PBS</i>	<i>Phosphate Buffered Saline</i>
<i>PCR</i>	<i>Polymerase Chain Reaction</i>
<i>PE</i>	<i>Phycoerythrin</i>
<i>PRRs</i>	<i>Pattern Recognition Receptors</i>
<i>Pts</i>	<i>Patients</i>
<i>QoL</i>	<i>Quality of Life</i>
<i>RBCs</i>	<i>Red Blood Cells</i>
<i>RDW</i>	<i>Red Cell Distribution Width</i>
<i>ROS</i>	<i>Reactive Oxygen Species</i>
<i>SCC-A</i>	<i>Side Scattering Areas</i>
<i>SD</i>	<i>Standard Deviation</i>
<i>SSC-W</i>	<i>Side Scatter Width</i>
<i>TBI</i>	<i>Transferrin Bound Iron</i>
<i>TCR</i>	<i>T-Cell Receptor</i>

List of Abbreviations (Cont...)

Abb.	Full term
<i>TDT</i>	<i>Transfusion Dependent Thalassemia</i>
<i>TF</i>	<i>Transferrin</i>
<i>TfR1</i>	<i>Transferrin Receptor1</i>
<i>TGF</i>	<i>Transforming Growth Factor</i>
<i>TH1</i>	<i>T Helper 1</i>
<i>TIBC</i>	<i>Total Iron Binding Capacity</i>
<i>TIF</i>	<i>Thalassemia International Federation</i>
<i>TLC</i>	<i>Total Leucocytic Count</i>
<i>TLR</i>	<i>Toll Like Receptor</i>
<i>TM</i>	<i>Thalassemia Major</i>
<i>TNF</i>	<i>Tumor Necrosis Factor</i>
<i>TS%</i>	<i>Transferrin Saturation percent</i>
<i>TTIs</i>	<i>Transfusion Transmitted Infections</i>
<i>VCAM-1</i>	<i>Vascular Cell Adhesion Molecule -1</i>
<i>WHO</i>	<i>World Health Organization</i>
<i>X</i>	<i>Mean</i>
<i>ZIP14</i>	<i>Zinc Importer Protein 14</i>

INTRODUCTION

β -thalassemia is a major public health problem in Egypt with particularly high incidence due to strong cultural preference for consanguineous marriages (*Adly & Ebeid, 2015*), and the high carrier rate of β -thalassemia that ranges from 9-16.4% with an overall rate of 12.36% (*Pessar, 2019*).

Iron overload, with subsequent multi organ damage, is the most important cause of morbidity and mortality in transfusion-dependent β -thalassemia patients (*Hoffbrand et al., 2012*). Infectious complications represent the second most common cause of mortality and the major cause of morbidity in β -thalassemia major (BTM). The increased susceptibility of these patients to infectious diseases has been attributed to the abnormalities of the immune system, which is evident by systemic inflammation and immune deficiency (*Elsayh et al., 2016*).

Monocyte is a professional innate sentinel cell that participates in various inflammatory conditions through activation and recruitment in response to many cytokines and also plays a major role in iron regulation (*Ghozali et al., 2018*). A study by *Kao et al. (2016)* has demonstrated that chronic iron overload causes lysosomal alkalization, impairs autophagic flux and lysosomal function of macrophages, and results in decreased bactericidal efficiency.