



Faculty of Post Graduate Childhood Studies
Department of Childhood Medical Studies

Evaluation of Serum Antioxidants and Immune Status in Children with β -Thalassemia Major Before and After Splenectomy

Thesis Submitted for Fulfilment of PHD Degree
Department of Childhood Medical Studies (Child Health and Nutrition)

BY

Ahmed Adel Fathy Mohamed

Msc pediatrics

Supervised by:

Dr. Gamal Sami Ali

*Professor of Pediatrics, Department of Childhood Medical Studies
Faculty of Postgraduate Childhood Studies, Ain Shams University*

Dr. Mohamed Khaled El-Menabbawy

*Professor of Child Health, Department of Child Health
National Research Center*

Dr. Fatma Abdel Rahman Elzaree

*Researcher of Child Health, Department of Child Health
National Research Center*

Dr. Reham Sabrey Abdel Aal

*Lecturer of Pediatrics, Department of Childhood Medical Studies
Faculty of Postgraduate Childhood Studies, Ain Shams University*

2019

Acknowledgement

Acknowledgement

I am grateful and thankful to God who makes all things possible. All praise is due to the Almighty. May Allah make our lives easier and grant.

I am greatly honored to express my deep gratitude and faithfulness to **PROF. DR. GAMAL SAMI ALI**, Professor of Pediatrics Medicine, Faculty of Postgraduate Childhood Studies, Ain Shams University, for his wisdom, invaluable advice, support, encouragement and the sharing of his expertise. Really, I learned a lot from him.

I wish to express my gratitude and appreciation to **PROF. DR. MOHAMED KHALED EL-MENABBAWY**, Professor of Child Health, National Research Center, for his great help, faithful advice, and kind support from the start and all through the work until its completion, and immense facilities he offered.

I wish to thank **DR. FATMA ABDEL RAHMAN ELZAREE**, Researcher of Child Health, National Research Center, for her generous help and goodness, meticulous revisions all through the work. She gave me much of her time, experience and support. Her valuable comments, efforts and collaboration were the causes to complete this work properly.

I would like to acknowledge the advice and guidance of **DR. REHAM SABREY ABDEL AAL**, Lecturer of Pediatric Medicine, Faculty of Postgraduate Childhood Studies, Ain Shams University, for her great support to me and for the great effort she made to make this work come to light ,many thanks for her kindness and support.

I deeply thank **DR. FATMA ABDEL HAMED IBRAHIM**, Researcher of Biochemistry, National Research Center, for her generous

effort she gave to make this work possible and for her generous support and encouragement to me.

I would like to thank my family members for supporting and encouraging me to pursue this degree.

Last, but certainly not least, I owe to the patients included in this study may God alleviate their sufferings and may all our efforts be just for their own benefit.

Abstract

Abstract

Background: β - thalasseмии are a group of inherited autosomal recessive hematological disorders due to defects in synthesis of β chains of hemoglobin; it results in red blood cell destruction with symptoms of anemia. Red blood cell destruction, repeated blood transfusion and bad compliance to routine use of iron chelator lead to iron accumulation in the heart, liver and endocrine organs.

Objectives: This study aimed at evaluating the effect of splenectomy on immunologic and antioxidant state by measuring the change in level of interleukin 6 and some antioxidant agents before and after splenectomy in thalassaemic patients.

Methods: 40 patients with confirmed homozygous β - thalassemia major were enrolled in this observational prospective cohort study before and after splenectomy that was conducted at Children Hospital Cairo University from December 2016 to December 2017.

Results: After splenectomy regarding immune status we found that there is a decrease in the mean Interleukin 6 by (36%) and IgM by (12.6%), regarding antioxidant status we observed a decrease in the mean MDA by (39%), increase in the mean level of total antioxidant by (68%) and the enzymatic antioxidant catalase enzyme was significantly increased by (72.5%).

Conclusions: After splenectomy there is improvement in the antioxidant capacity of plasma in terms of increasing serum total antioxidants level, catalase enzyme and there is deterioration of immune status in the form of decrease in the mean level of Interleukin 6, with decrease in the mean level of IgM.

Key words: β -thalassemia major - Oxidative stress - Antioxidant enzymes- Splenectomy - Interleukin 6.

List of contents

- List of abbreviations.....I
- List of tables.....III
- List of figures.....V
- Introduction.....1
- Aim of study.....4

Review of the literature

Chapter I: Beta-Thalassemiias

- Definition5
- Geographic distribution6
- Pathophysiology10
- Clinical features12
- Diagnosis.....15
- Management16
- Prevention.....23

Chapter II: Antioxidants and Immunity in β -Thalassemia major

- Definition25
- Classification27
- Antioxidant supplementation 31
- Role of antioxidant in thalassemia.....34
- Immune defect in thalassemia.....38
- Type of change in immune cells.....39

Chapter III: Splenectomy in β -Thalassemia major

- Indication of splenectomy.....44
- Complication of splenectomy.....45
- Patients and methods.....49
- Results.....55
- Discussion.....71

- **Summary and conclusions.....80**
- **Recommendations.....84**
- **References.....85**
- **Arabic summary**

Lists of Abbreviation

α	Alpha
β	Beta
γ	Gamma
δ	Delta
ABGs	Arterial blood gases
ALP	Alkaline phosphatase
ANC	Absolute neutrophilic count
APS	American pain society
BMI	Body mass index
BMT	Bone marrow transplantation
COX	Cyclo-oxygenase
CT scan	Computerized tomography scans
CVS	Chorionic villous sampling
DFO	Deferoxamine
DFP	Deferiprone
DtaP	Diphtheria, Tetanus, acellular Pertussis
EACA	Epsilon amino caproic acid
EKG	Electrocardiogram
EMA	Food and Drug Administration
FDA	European Medicines Agency
GMP	Gaunosine mono phosphate
GVHD	Graft verses host disease
G6PD	Glucose 6 phosphates deficiency
Hb	Hemoglobin
Hb A	Adult hemoglobin
α -HBD	α -Hydroxybutyric dehydrogenase
Hb F	Fetal hemoglobin
Hb S	Sickle hemoglobin
HCT	Hematocrit
H. influenza	Haemophilus influenza
HIB	Haemophilus influenza type B vaccine
HIV	Human immune deficiency virus
HPLC	High performance liquid chromatography
HPHP	Hereditary persistent fetal haemoglobin
HU	Hydroxyurea therapy
ICAM-4	Intercellular adhesion molecule-4
IEF	Isoelectric focusing
IL	Interleukin
IQ	Intelligence quotient

ISC	Irreversibly sickled cells
IUHSCTx	In utero hematopoietic stem cell transplantation
LC	Laparoscopic cholecystectomy
MCA	Major carotid artery
MCH	Mean corpuscular hemoglobin
MCHC	Mean corpuscular hemoglobin concentration
MCV	Mean corpuscular volume
MMR	Measles, Mumps, Rubella
MRA	Magnetic resonance angiography
MRI	Magnetic resonance imaging
MTD	Maximum tolerated dose
MSH	The Multicenter Study of Hydroxyurea in SCA.
NHLBI	National Heart, Lung and blood institute
NO	Nitric oxide
NSAIDs	Nonsteroidal anti-inflammatory drugs
PCA	Patient controlled analgesia
PFT	Pulmonary function testing
PGD	Preimplantation genetic diagnosis
Polio	Oral polio vaccine
PON	Paraoxonase
RBC	Red blood cells
ROS	Reactive oxygen species
SCA	Sickle cell anemia
SB	Sickle beta thalassemia
SCD	Sickle cell disease
SCT	Stem cell transplantation
SOD	Superoxide dismutase
TBV	Total blood volume
TI	Thalassemia intermedia
TM	Thalassemia major
UTI	Urinary tract infection
VCAM-1	Vascular cell adhesion molecule-1
VOC	Vaso- occlusive crises
WBC	White blood cells

List of Tables

Table In Review	Subject	Page
Table A	Human antioxidants; their mode of action	37
Table In Results	Subject	Page
Table 1	Distribution of gender and age of studied patients	55
Table 2	Distribution of under nutrition among studied patients	56
Table 3	Comparison between age groups of patients and presence of malnutrition	57
Table 4	Comparison between the mean level of Hemoglobin before and after splenectomy among studied patients	58
Table 5	Comparison between the mean level of Platelets before and after splenectomy among studied patients	59
Table 6	Comparison between the mean level of Reticulocytes before and after splenectomy among studied patients	60
Table 7	Comparison between the mean level of ferritin before and after splenectomy among studied patients	61
Table 8	Comparison between the mean level of WBCs before and after splenectomy among studied patients	62
Table 9	Comparison between the mean level of liver function before and after splenectomy among studied patients	63
Table 10	Comparison between the mean level of malondialdehyde, before and after splenectomy among studied patients	64
Table 11	Comparison between level of total antioxidant capacity before and after splenectomy among studied patients	65
Table 12	Comparison between the mean level of catalase before and after splenectomy among studied patients	66
Table 13	Comparison between level of Glutathione transferase before and after splenectomy among studied patients	67
Table 14	Comparison between the mean level of interleukin 6 before and after splenectomy among studied patients	68

Table 15	Comparison between the mean level of immunoglobulin M before and after splenectomy among studied patients	69
Table 16	Comparison between level of complement 3 parameters before and after splenectomy among studied patients	70

List of Figures

Figure		Page
Figure 1	Pathophysiology of thalassemia	11
Figure 2	Complication of beta thalassemia	14
Figure 3	Distribution of gender of studied patients	55
Figure 4	Distribution of under nutrition among studied patients	56
Figure 5	Comparison between age groups of patients and presence of malnutrition	57
Figure 6	Comparison between the mean level of Hemoglobin before and after splenectomy among studied patients	58
Figure 7	Comparison between the mean level of Platelets before and after splenectomy among studied patients	59
Figure 8	Comparison between the mean level of Reticulocytes before and after splenectomy among studied patients	60
Figure 9	Comparison between the mean level of ferritin before and after splenectomy among studied patients	61
Figure 10	Comparison between the mean level of WBCs before and after splenectomy among studied patients	62
Figure 11	Comparison between the mean level of liver function before and after splenectomy among studied patients	63
Figure 12	Comparison between level of malondialdehyde, before and after splenectomy among studied patients	64
Figure 13	Comparison between level of total antioxidant capacity before and after splenectomy among studied patients	65

Figure 14	Comparison between the mean level of catalase before and after splenectomy among studied patients	66
Figure 15	Comparison between level of Glutathione transferase before and after splenectomy among studied patients	67
Figure 16	Comparison between the mean level of interleukin 6 before and after splenectomy among studied patients	68
Figure 17	Comparison between the mean level of immunoglobulin M before and after splenectomy among studied patients	69
Figure 18	Comparison between level of complement 3 parameters before and after splenectomy among studied patients	70

Introduction & Aim of Work