

Study of the Alterations of Platelet Parameters and Functions in Children and Adolescent with Iron Deficiency Anemia and Response to Therapy

Thesis

Submitted for the partial fulfillment of M.D. degree
in Pediatrics

Presented by

Heba Gomaa abd El Raheem

M.B.B.Ch., M.Sc.Pediatrics
Faculty of Medicine - Ain Shams University

Under Supervision of

Prof. Dr./ Galila Mohamed Mokhtar

Professor of Pediatrics
Faculty of Medicine, Ain Shams University
Head of Pediatric Department and Hematology-oncology Unit

Prof. Dr./ Wafaa Ezzat Ibrahim

Professor of Pediatrics
Faculty of Medicine, Ain Shams University

Prof. Dr./ Nevine Ahmed Kassim

Professor of Clinical Pathology
Faculty of Medicine, Ain Shams University

Dr. /Iman Ahmed Ragab

Lecturer of Pediatrics
Faculty of Medicine, Ain Shams University

Dr. /Abeer Attia Saad

Lecturer of Clinical Pathology
Faculty of Medicine, Ain Shams University

**Faculty of Medicine
Ain Shams University
2013**

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

﴿ قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا
إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ الْعَلِيمُ
الْحَكِيمُ ﴾

صدق الله العظيم

سورة البقرة الآية (٣٢)



Acknowledgement

*Thanks are given to **ALLAH** the source of all knowledge for blessing this work till it has come to an end.*

*I would like to express my deepest thanks to **Prof. Dr. Galila Mohamed Mokhtar**, Professor of Pediatrics, Faculty of Medicine, Ain Shams University, for her kind support guidance and valuable remarks. I am profoundly grateful for her continuous close supervision and constant help.*

*I would also like to express my deepest thanks and gratitude to **Prof. Dr. Wafaa Ezzat Ibrahim**, Professor of Pediatrics, Faculty of Medicine, Ain Shams University for his generous help, continuous encouragement and stimulating remarks throughout the study.*

*I would also like to express my great gratitude to **Dr. Nevine Ahmed Kassim**, Professor of clinical pathology, Faculty of Medicine, Ain Shams University for her valuable comments, knowledge, experience and hand necessary for achieving this work.*

*Many thanks to **Dr. Iman Ahmed Ragab**, Lecturer of Pediatric, Faculty of Medicine, Ain Shams University and **Dr. Abeer Attia Saad**, Assistant professor of clinical pathology, Faculty of medicine, Ain Shams University for their generous help, supervision, and extreme kindness through out the work.*

Many thanks to my patients who helped me in my study.

Last but not least, I would like to thank my family who encouraged and supported me all the time, to them I dedicate this work.

Contents

<i>Subject</i>	<i>Page No.</i>
List of Abbreviations.....	i
List of Tables.....	iii
List of figures.....	iv
Protocol.....	
Abstract.....	I
Introduction.....	1
Aim of The Work.....	3
Review of Literature	
Iron and Iron Deficiency Anemia.....	4
Platelet and platelet function Assessment.....	32
Iron and Platelet Parameters.....	53
Patients and Methods	63
Results.....	85
Discussion.....	109
Summary And Conclusion.....	118
Recommendations.....	121
References.....	122
Appendix.....	I
Arabic summary.....	—

List of Abbreviations

AA	: Arachidonic acid
AAP	: American Academy of Pediatrics
ACS	: Acute coronary syndrome
ADP	: Adenosine diphosphate
aPTT	: activated partial thromboplastin time
At	: Adequate Intake
BCSH	: British Committee for Standard Hematology
BT	: Bleeding time
CADP	: Collagen/Adenosine diphosphate
CAMP	: Cyclic adenosine monophosphate
CBC	: Complete blood count
CEPI	: Collagen/Epinephrine
CLSI	: Clinical and laboratory Standard Institute
CNS	: Central nervous system
CT	: Closure time
CVS	: Cardiovascular system
DALY's	: Disability Adjusted Life Years
DMT	: Divalent metal transporter-1
ELISA	: Enzyme-linked immuno sorbent assay
EPI	: Epinephrine
Epo	: Erythropoietin
ESA	: Erythropoietin stimulating agent
Fe³⁺	: Ferric iron
GIT	: Gastrointestinal tract
GV	: Growth velocity
Hb	: Hemoglobin
HCT	: Hematocrit

List of Abbreviations *(Cont...)*

HR	: Heart rate
IDA	: Iron deficiency anemia
IEG	: International Expert Group
IMP	: Integrin-mobilferrin pathway
IRIDA	: Iron refractory anemia
ISTH	: International Society on Thrombosis and hemostasis
Kcal	: Kilo calories
LDCs	: Lesser-developed countries
LTA	: Light transmission aggregometry
MCH	: Mean corpuscular hemoglobin
MCHC	: Mean corpuscular hemoglobin concentration
MCV	: Mean corpuscular volume
mL	: Milliliter
MPV	: Mean platelet volume
OCD	: Obsessive compulsive disorder
PF4	: Platelet factor 4
PFA	: Platelet function analyzer
PFA100	: Platelet function analyzer 100
plt	: Platelet
ppm	: Parts per million
PPP	: Platelet-poor plasma
PRP	: Platelet-rich plasma
PT	: Prothrombin time
PTG	: Beta-thromboglobulin
RBC	: Red blood cell
RDA	: Recommended Dietary Allowance
RDW	: Red cell distribution width
RETICs	: Reticulocytes

List of Abbreviations *(Cont...)*

RR	: Respiratory rate
SD	: Standard deviation
SES	: Socioeconomic standards
SIT	: Stimulators of iron transport
SSC	: Scientific and Standardization Committee
Temp	: Temperature
TfR	: Transferrin receptor
TIBC	: Total iron binding capacity
TMB	: Tetramethylbenzidine
UIBC	: Unsaturated Iron-binding capacity
vWD	: von Willebrand Disease
WBA	: Whole blood aggregometer
WBC	: White blood count
WHO	: World Health Organization

List of Tables

<i>Tab. No.</i>	<i>Title</i>	<i>Page No.</i>
<u>Review of Literature</u>		
Table (1):	Recommended dietary allowance of iron by age and sex.....	5
Table (2):	Dietary sources of iron.	6
Table (3):	Most common causes of iron deficiency anemia.....	14
Table (4):	Anemia Prevalence and Number of Individuals Affected.....	16
Table (5):	Differential diagnosis of iron deficiency anemia.....	22
Table (6):	Iron preparation form	27
Table (7):	Most common causes of failure of oral iron therapy.	28

List of Tables (Cont...)

<i>Tab. No.</i>	<i>Title</i>	<i>Page No.</i>
<u>Results:</u>		
Table (1):	Comparison between patients and control group regarding age, sex, socioeconomic standard (SES).	85
Table (2):	Comparison between patients and control group regarding hematological symptoms.	86
Table (3):	Comparison between patients and control group regarding GIT symptoms.	87
Table (4):	Comparison between patients and control group regarding CNS symptoms.	87
Table (5):	Comparison between patients and control group regarding CVS symptoms.	88
Table (6):	Comparison between patients and control regarding others symptoms.	88
Table (7):	Comparison between patients and control group regarding anthropometric measures.....	89
Table (8):	Comparison between patients and control group regarding vital data.....	90
Table (9):	Comparison between patients and control group regarding hematological signs.....	90
Table (10):	Comparison between patients and control group regarding GIT signs.	91

List of Tables (Cont...)

<i>Tab. No.</i>	<i>Title</i>	<i>Page No.</i>
<u>Results (Cont...):</u>		
Table (11):	Comparison between patients and control group regarding others signs.	91
Table (12):	Comparison between patients and control group regarding complete blood picture (CBC).	92
Table (13):	Comparison between patients and control group regarding platelet aggregation	94
Table (14):	Comparison between patients and control regarding PFA-100 closure time.....	95
Table (15):	Comparison between hematological symptoms in patients before and after treatment.	96
Table (16):	Comparison between vital signs (HR, RR and body temperature) in patients before and after treatment.	97
Table (17):	Comparison between anthropometric measures in patients before and after treatment.	98
Table (18):	Comparison between complete blood count in patients before and after treatment.	100
Table (19):	Comparison between iron profile in patients before and after treatment.....	102
Table (20):	Comparison between platelet aggregation in patients before and after treatment.	103
Table (21):	Comparison between PFA 100 closure time in patients before and after treatment.	104

List of Tables (Cont...)

<i>Tab. No.</i>	<i>Title</i>	<i>Page No.</i>
<u>Results (Cont...):</u>		
Table (22):	Correlation between PFA 100, platelet aggregation induced by (ADP, epinephrine and ristocetin) and complete blood picture parameter in patients before treatment.....	105
Table (23):	Correlation between PFA 100, platelet aggregation induced by (ADP, epinephrine and ristocetin) and iron profile in patients before treatment.	107
Table (24):	Correlation between PFA 100 and platelet aggregation induced by (ADP, epinephrine and ristocetin) in patients before treatment.....	108

List of Figures

<i>Figure No.</i>	<i>Title</i>	<i>Page No.</i>
<u>Review of Literature</u>		
Figure (1):	Balance between iron absorption and body losses.....	8
Figure (2):	Regulation of iron absorption via absorptive cells in proximal small intestine.....	10
Figure (3):	Factor affecting iron absorption	11
Figure (4):	Mechanism of iron absorption.....	11
Figure (5):	Severity of iron deficiency anemia worldwide	15
Figure (6):	The CBC demonstrates a decreased MCV in association with the decreased Hb and HCT in this case of iron deficiency anemia and peripheral blood smear demonstrating changes with iron deficiency anemia	20
Figure (7):	The sequence of events (left to right) that occur with gradual depletion of body stores of iron	21
Figure (8):	Diagnostic plot for identifying the different erythropoietic states with therapeutical implications for the treatment of different phases of iron deficiency	31
Figure (9):	Image from a light microscope (40×) from a peripheral blood smear surrounded by red blood cells.....	32
Figure (10):	Platelet production from bone marrow.....	33

List of Figures (Cont...)

<i>Figure No.</i>	<i>Title</i>	<i>Page No.</i>
Figure (11):	Mechanism of primary hemostasis	35
Figure (12):	Algorithm for evaluating a platelet dysfunction in patient with bleeding disorder with normal or elevated platelet count	36
Figure (13):	Algorithm for evaluating a platelet disorder in patient with decreased platelet count.....	37
Figure (14):	Algorithm for evaluating a platelet disorder in patient with thrombocytopenia and normal platelet morphology.....	38
Figure (15):	The in vivo bleeding time performed with a Simplate II® device.....	42
Figure (16):	Platelet function analyser. The PFA-100_ device.....	43
Figure (17):	Normal closure time using PFA 100.	44
Figure (18):	Closure time in relation to platelet count and hematocrit	46
Figure (19):	Stages for platelet aggregations.....	48
Figure (20):	Multiple forms of platelet aggregometer	50
Figure (21):	Platelet function analyzer – 100 (PFA-100).....	79

List of Figures (Cont...)

<i>Figure No.</i>	<i>Title</i>	<i>Page No.</i>
<u>Results:</u>		
Figure (1):	Comparison between patients and control group regarding bleeding manifestations.	86
Figure (2):	Comparison between patients and control regarding SDS for height.	89
Figure (3):	Comparison between patients and control group regarding complete blood picture (CBC).....	93
Figure (4):	Comparison between patients and control regarding platelet aggregation induced by ADP, epinephrine and ristocetin.	94
Figure (5):	Comparison between patients and control regarding PFA100 values.....	95
Figure (6):	Comparison between bleeding tendency in patients before and after treatment.....	96
Figure (7):	Comparison between vital signs(HR, RR and body temperature) in patients before and after treatment.	97
Figure (8a):	Comparison between SDS for weight in patients before and after treatment.	98
Figure (8b):	Comparison between SDS for height in patients before and after treatment	99
Figure (9):	Comparison between complete blood picture (CBC) in patients before and after treatment.	101

List of Figures (Cont...)

<i>Figure No.</i>	<i>Title</i>	<i>Page No.</i>
Results (Cont...)		
Figure (10):	Comparison between serum iron, TIBC and serum ferritin in patients before and after treatment.	102
Figure (11):	Comparison between platelet aggregation induced by ADP and Epinephrine in patients before and after treatment.....	103
Figure (12):	Comparison between PFA 100 values in patients before and after treatment	104
Figure (13):	Correlation between platelet aggregation induced by ADP and mean values of RBCs in patients before treatment.....	106
Figure (14):	Correlation between platelet aggregation induced by ADP and mean values of serum ferritin in patients before treatment.....	107