

# **Effect of Breast Milk Interleukin-7 on Thymic Development in Young Infants**

Thesis

Submitted for Partial Fulfillment of MD Degree  
in Pediatrics

By

*Amira Fouad Ahmed El-Said*  
*M.B., B.Ch. (2006), MS. Pediatrics (2012)*

Under the Supervision of

**Prof. Elham Mohammad Hossny**  
*Professor of Pediatrics*  
*Faculty of Medicine - Ain Shams University*

**Dr. Dalia Helmy El-Ghoneimy**  
*Assistant Professor of Pediatrics*  
*Faculty of Medicine - Ain Shams University*

**Dr. Rasha Hassan El-Owaidy**  
*Lecturer of Pediatrics*  
*Faculty of Medicine – Ain Shams University*

**Dr. Mohammad Gamal El-Deen Abd-Elmottaleb**  
*Assistant Professor of Radiology*  
*Faculty of Medicine – Ain Shams University*

**Dr. Mohammad Tareef Hamza**  
*Assistant Professor of Clinical Pathology*  
*Faculty of Medicine – Ain Shams University*

Faculty of Medicine  
Ain Shams University  
**2017**



بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قار

الْمُحَلِّاتُكَ لَا هَالِكُ لَنَا  
أَلَا مَا هَالَكُنَا أَنْتَ  
الْعَظِيمُ الْعَظِيمُ

صدقة الله العظيم

سورة البقرة الآية: ٣٢



A decorative border with a repeating pattern of stylized flowers and leaves in red, green, and blue, framing the central text.

## *Dedication*

To:

*My mum,  
My Husband & My kids  
for their endless love, support,  
and continuous care  
&  
Soul of my father  
My whole Family*





## Acknowledgments

*First and foremost, I feel always indebted to Allah  
the Most Beneficent and Merciful.*

*I wish to express my deepest thanks, gratitude and appreciation to  
**Prof. Elham Mohammad Hossny**, Professor of Pediatrics, Faculty of  
Medicine, Ain Shams University, for her meticulous supervision, valuable  
instructions and generous help.*

*Special thanks are due to **Dr. Dalia Helmy El-Ghoneimy**,  
Assistant Professor of Pediatrics, Faculty of Medicine, Ain Shams  
University, for her sincere efforts and fruitful encouragement all through this  
work.*

*I am deeply thankful to **Dr. Rasha Hassan El-Owaidy**, Lecturer of  
Pediatrics, Faculty of Medicine, Ain Shams University, for her great help,  
outstanding support, active supervision and guidance.*

*I can hardly find the words to express my gratitude to **Dr.  
Mohammad Gamal El-Deen Abd-Elmottaleb**, Assistant Professor of  
Radiology, Faculty of Medicine, Ain Shams University, for his supervision  
and continuous help throughout the radiological part of this work.*

*I would like also to express my sincere appreciation and gratitude to  
**Dr. Mohammad Tareef Hamza**, Assistant Professor of Clinical  
Pathology, Faculty of Medicine, Ain Shams University, for his continuous  
directions and support throughout the laboratory part of this work.*

*I would like to thank **the mothers of the enrolled infants** for  
giving the consent, trust and support that led to accomplishment of this  
work.*

**Amira Fouad Ahmed**





# List of Contents

Title	Page No.
List of Abbreviations.....	i
List of Tables .....	iv
List of Figures .....	vii
Introduction and Aim of the work .....	1
Thymus gland.....	4
Structure of the thymus gland.....	4
Function of the thymus gland .....	8
Factors affecting thymus gland size .....	12
Involution of the thymus gland.....	14
Evaluation of the normal thymus gland.....	16
Human breast milk immunology.....	21
Immune factors in human milk .....	22
Interleukin-7 (IL-7) .....	29
Biology of IL-7 and its signaling.....	29
Function of IL-7 in T cell-mediated immune response and the underlying mechanisms .....	34
Role of IL-7 in B- cell development.....	38
IL-7 and primary immune deficiency .....	38
Subjects and methods .....	40
Results.....	47
Discussion.....	67
Recommendations .....	76
Summary .....	77
References .....	80
Arabic summary	



# List of Abbreviations

Abbreviation	Full term
<i>AAP</i> .....	<i>American Academy of Pediatric</i>
<i>Akt/PKB</i> .....	<i>(Akt/PKB) Serine/Threonine Protein Kinase B</i>
<i>ALC</i> .....	<i>Absolute Lymphocyte Count</i>
<i>BAK</i> .....	<i>Bcl-2 Homologous Antagonist Killer</i>
<i>BAX</i> .....	<i>Bcl-2 Associated X Protein</i>
<i>BC</i> .....	<i>B cells</i>
<i>BCL-2</i> .....	<i>B cell Lymphoma 2</i>
<i>CBC</i> .....	<i>Complete Blood Count</i>
<i>CDC</i> .....	<i>Centers for Disease Control and Prevention</i>
<i>CEC</i> .....	<i>Cortical Epithelial Cell</i>
<i>CICD</i> .....	<i>Cytokine Induced Cell Death</i>
<i>CMJ</i> .....	<i>Cortico-Medullary Junction</i>
<i>CT</i> .....	<i>Computed Tomography</i>
<i>CTECs</i> .....	<i>Cortical Thymic Epithelial Cells</i>
<i>DCs</i> .....	<i>Dendrite Cells</i>
<i>DN</i> .....	<i>Double Negative</i>
<i>DP</i> .....	<i>Double Positive</i>
<i>EBF</i> .....	<i>Exclusively Breast Fed</i>
<i>EGF</i> .....	<i>Epidermal Growth Factor</i>
<i>ETP</i> .....	<i>Early Thymic Progenitor</i>
<i>F</i> .....	<i>One Way ANOVA</i>
<i>FF</i> .....	<i>Formula-Fed</i>
<i>GAS</i> .....	<i>Gamma-Activated Sequence</i>
<i>gc Chain</i> .....	<i>Common Gamma Chain</i>
<i>G-CSF</i> .....	<i>Granulocyte Colony Stimulating Factor</i>
<i>HIV</i> .....	<i>Human Immune Deficiency Virus</i>
<i>HPE</i> .....	<i>Homeostatic Peripheral Expansion</i>
<i>Ig</i> .....	<i>Immunoglobulin</i>
<i>IgG</i> .....	<i>Immunoglobulin G</i>
<i>IgM</i> .....	<i>Immunoglobulin M</i>
<i>IL</i> .....	<i>Interleukin</i>



# List of Abbreviations Continued

Abbreviation	Full term
<i>IL-7Ra</i> .....	<i>Interleukin 7 Receptor Alpha</i>
<i>INF<math>\gamma</math></i> .....	<i>Interferon Gamma</i>
<i>IREs</i> .....	<i>Internal Ribosome Entry Sites</i>
<i>ISP</i> .....	<i>Immature Single Positive</i>
<i>JaK</i> .....	<i>Janus Kinase</i>
<i>KDa</i> .....	<i>Kilodalton</i>
<i>MCl</i> .....	<i>Myeloid Leukemia Cell Differentiation Protein</i>
<i>MEC</i> .....	<i>Medullary Epithelial Cells</i>
<i>MF</i> .....	<i>Macrophage Migratroy Inhibitory Factor</i>
<i>MRI</i> .....	<i>Magnetic resonant Imaging</i>
<i>mTECs</i> .....	<i>Medulley Thymic Epithelial Cells</i>
<i>MUC-1</i> .....	<i>Mucin 1</i>
<i>NEATc1</i> .....	<i>Nuclear Factor of Activated T Cells</i>
<i>NK</i> .....	<i>Natural Killer</i>
<i>PI3K</i> .....	<i>Phosphatidyl inositol 3-Kinase</i>
<i>PI3K-AKT</i> .....	<i>SerineThreonine Protein kinase B and Phophatidyle inositol 3 Kinase</i>
<i>RTes</i> .....	<i>Recent Thymic Emigrants</i>
<i>S IgA</i> .....	<i>Secretory Immunoglobulin A</i>
<i>SCID</i> .....	<i>Severe Combined Immunodeficiency</i>
<i>SD</i> .....	<i>Standard Deviation</i>
<i>SP</i> .....	<i>Single Positive</i>
<i>STAT</i> .....	<i>Signal Transducers and Activator of Transcription</i>
<i>TCRs</i> .....	<i>T cell Receptors</i>
<i>TEC</i> .....	<i>Thymic Epithelial Cells</i>
<i>TGF</i> .....	<i>Tumor Growth Factor</i>
<i>TGF<math>\beta</math></i> .....	<i>Tumor Growth Factor Beta</i>
<i>Th</i> .....	<i>T helper</i>
<i>TLC</i> .....	<i>Total Leucocytic Count</i>
<i>TNF</i> .....	<i>Tumor Necrosis Factor</i>
<i>TRECs</i> .....	<i>T cell Receptor Excision Circles</i>

# List of Abbreviations Continued

Abbreviation	Full term
<i>Tyr 371</i> .....	<i>Tyrosine 371</i>
<i>US</i> .....	<i>Ultrasonography</i>
<i>WHO</i> .....	<i>World Health Organization</i>
<i>γδ lymphocyte</i> .....	<i>Gamma Delta Lymphocytes</i>

# List of Tables

Table No.	Title	Page No.
Table (1):	Mean and median thymic indices in infants with different types of feeding.....	18
Table (2):	Summary of immune factors and their function in human breast milk.....	22
Table (3):	Variation of the clinicodemographic and the studied laboratory parameters among the three studied groups at enrollment at the age of 2 months.....	48
Table (4):	Variation of thymic indices with gender among the three studied groups at the age of enrollment (2 months) .....	49
Table (5):	Correlations between thymic index and the studied leukocyte counts in the exclusively breast fed group at 2 months of age.....	50
Table (6):	Correlations between thymic index and the studied leukocyte counts among formula fed group at the age of 2 months .....	51
Table (7):	Correlations between thymic index and the studied leukocyte counts in the mixed fed group at the age of 2 months.....	51
Table (8):	Correlations between breast milk IL-7 levels, leukocyte counts and thymic index in the exclusively breast fed infants at the age of 2 months .....	52