



شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكرو فيلم

بسم الله الرحمن الرحيم



HANAA ALY



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شبكة المعلومات الجامعية التوثيق الإلكتروني والميكروفيلم



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جامعة عين شمس التوثيق الإلكتروني والميكروفيلم

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Serum Soluble Cytotoxic T-Lymphocyte-Associated Antigen 4 in Children and Adolescents with Autoimmune Cytopenia

Thesis

Submitted for Partial Fulfillment of Master Degree in
Paediatrics

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2021**

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

لسببنا انك لا تعلم لنا
إلا ما علمتنا إنك أنت
العليم الكبير

صدق الله العظيم

سورة البقرة الآية: ٣٢



Acknowledgement

*First of all, all gratitude is due to **Allah** Almighty, for blessing this work, until it has reached its end, as a part of his generous help, throughout my life.*

*Really I can hardly find the words to express my gratitude to **Dr. Nayera Hazaa Khalil El-Sherif**, Professor in department of Pediatrics, Faculty of Medicine, Ain Shams University, Cairo-Egypt, for her supervision, continuous help, encouragement throughout this work and tremendous effort she has done in the meticulous revision of the whole work. It is a great honor to work under her guidance and supervision.*

*I would like also to express my sincere appreciation and gratitude to **Dr. Mona Fathey AbdelFattah Hassan**, Professor in Department of Clinical Pathology, Faculty of Medicine, Ain Shams University, Cairo-Egypt, for her continuous directions and support throughout the whole work.*

*I cannot forget the great help of **Dr. Sara Mostafa Makkeyah**, lecturer in Department of Pediatrics, Faculty of Medicine, Ain Shams University, Cairo-Egypt, for her invaluable efforts, tireless guidance and for her patience and support to get this work into light.*

*I'm grateful to the **patients** for their participation and cooperation in this research making it possible.*

*I am extremely sincere to **my family** who stood beside me throughout this work giving me their support.*

Marwa Gamal Mohamed Ibrahim

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List of Abbreviations

<i>Abbr.</i>	<i>Full-term</i>
ADCC	: Antibody-dependent cell-mediated cytotoxicity
APC	: Antigen presenting cells
AIHA	: Autoimmune hemolytic anemia
AIN	: Autoimmune neutropenia
ALPS	: Autoimmune lymphoproliferative syndrome
Bcl-xL	: B-cell lymphoma-extra large
BTLA	: B- and T- lymphocyte attenuator
CD4	: Cluster of differentiation 4
CD8	: Cluster of differentiation 8
CAD	: Cold agglutinin disease
CVID	: Common variable immunodeficiency syndrome
CTLA-4	: Cytotoxic T-lymphocyte-associated protein 4
DAT	: Direct anti-globulin test
EV	: Evans syndrome
FOXP3	: Forkhead box P3
FAS	: First apoptosis signal receptor
TH	: Helper T cells
HSCT	: Hematopoietic stem cell transplantation
HVEM	: Herpes virus entry mediator
ITP	: Immune thrombocytopenic purpura
IDO	: Indoleamine 2,3- dioxygenase
ICOS	: Inducible T-cell costimulatory
IFNγ	: Interferon gamma

JAK2	: Janus Kinase 2 gene
IL	: Interleukin
LATAIE	: LRBA deficiency with autoantibodies, T regulatory (Treg) cell defects, autoimmune infiltration, and enteropathy
LRBA	: Lipo-polysaccharide-responsive-vesicle-trafficking-Beige-like-Anchor protein
LFA-1	: Lymphocyte function associated antigen 1
MHC	: Major histocompatibility complex
NK	: Natural killer cells
GP	: Platelet glycoprotein
PD-1	: Programmed cell death protein 1
PP2A	: Protein phosphatase 2A
T_{REG} cells	: Regulatory T-cells
SHP-2	: Src-homology-containing tyrosine phosphatase-2
sCTLA-4	: Soluble Cytotoxic T-lymphocyte-associated protein 4
SD	: Standard deviation
SPSS	: Statistical package for social science
TEC	: Thymic epithelial cells
TCR	: T cell receptor
TGFβ	: Transforming growth factor beta
TFH	: T follicular helper cells
TIM-3	: T-cell immunoglobulin and mucin-domain containing-3

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Abstract

Background: serum soluble cytotoxic t-lymphocyte-associated antigen 4 (sCTLA-4) exerts either inhibitory or stimulatory effect depending on the activation state of the immune response. Several studies reported the observation of elevated levels of sCTLA-4 in several autoimmune diseases. **Aim of the work:** to measure the serum level of sCTLA-4 in patients with immune cytopenia (AIHA, EVANS, ALPS, AND ITP). **Patients and methods:** forty-seven children and adolescents with immune cytopenias were recruited and assessed for eligibility at the pediatric hematology/ oncology clinic, Ain Shams University children's hospital and compared with age and gender matched 47 healthy subjects. **Results:** immune-cytopenic patients group have statistically significant ($P < 0.01$) higher serum sCTLA-4 levels median (IQR) 14 (10 – 20) compared to controls median (IQR) 3 (2 - 6). On the other hand, no significant difference was found as regards levels of sCTLA-4 between sera of ITP, AIHA and ALPS patients ($P > 0.05$). Serum sCTLA-4 was inversely related to the age at diagnosis and positively related to disease duration. Our results demonstrated the presence of negative correlation between sCTLA-4 and current laboratory hemoglobin levels ($P = 0.031$) and positive correlation to the current reticulocyte count ($P = 0.004$), indirect bilirubin ($P = 0.003$) and lactate dehydrogenase ($P = 0.014$). **Conclusion:** soluble form of ctla4 (sCTLA-4) presents in elevated levels in the sera of children and adolescents who have immune cytopenia including AIHA/EVANS, ITP and ALPS compared to healthy control group which emphasis its role in the pathogenesis of immune cytopenia.

Key words: serum, soluble cytotoxic t-lymphocyte-associated antigen 4 children, adolescents autoimmune cytopenia.