بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

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جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

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MONA MAGHRABY

Role of Circulating Myeloid-Derived Suppressor Cells in Pathogenesis of Immune Thrombocytopenia in Children and Adolescents

A Thesis

Submitted for partial fulfillment of Master degree in Pediatrics

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✍ **Fatma Ahmed Bayomi**

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List of Abbreviations

Abbr.		Full-term
ACK	**:**	Ammonium Chloride Potassium
ANA	**:**	Anti-Nuclear Antibodies
APS	**:**	The antiphospholipid syndrome
Arg1	**:**	Arginase 1
ASH	**:**	The American Society of Hematology
BAFF	**:**	B-lymphocyte Activating Factor
BM	**:**	Bone marrow
BMMCs	**:**	Bone Marrow Mononuclear Cells
BSA	**:**	Bovine Serum Albumin
Cag A	**:**	Cytotoxin - associated gene A
CIN	**:**	Chronic Idiopathic Neutropenia
CMPs	**:**	Common Myeloid Progenitors.
CMV	**:**	Cytomegalovirus
COVID 19	**:**	Corona Virus Disease
COX1	**:**	Cyclo-Oxygenase 1
CRP	**:**	C- Reactive Protein
CSFs	**:**	Colony-Stimulating Factors
DC	**:**	Dendritic Cell
DXM	**:**	Dexamethasone
EBV	**:**	Epstein Barr Virus
EDTA	**:**	Ethylene Diamine Tetra Acetic acid
ESR	**:**	Erythrocyte Sedimentation Rate
eTPO	**:**	Endogenous Thrombopoietin
FcγR	**:**	Fc Gamma Receptor
fl	**:**	Femtoliters

g/dl	**:**	Grams per decilitre
GCs	**:**	Glucocorticoids
GPs	**:**	Platelet Membrane Glycoproteins
H Pylori	**:**	Helicobacter pylori
HCV	**:**	Hepatitis C Virus
HD-DXM	**:**	High Dose Dexamethasone
HIV	**:**	Human Immunodeficiency Virus
HLA	**:**	Human leucocyte antigen
HPA	**:**	Human platelet antigen
HRQoL	**:**	Health Related Quality of Life
HSCT	**:**	Hematopoietic Stem Cell Transplantation
ICIs	**:**	anti-Checkpoint Inhibitors
IDO	**:**	Indoleamine 2,3 Di-Oxygenase
IgG	**:**	Immunoglobulin G
IgM	**:**	Immunoglobulin M
IL1-RA	**:**	Interleukin 1 Receptor Antagonist
IL10	**:**	Interleukin 10
ITP	**:**	Immune thrombocytopenia
IVIG	**:**	Intravenous Immunoglobulins
IWG	**:**	International Working Group
MCV	**:**	Mean Corpuscular Volume
MDSCs	**:**	Myeloid-Derived Suppressor Cells
MHC	**:**	Major Histocompatibility Complex
MICA	**:**	MHC Ⅰ chain related gene A
Mi RNA	**:**	Micro RNA
ML	**:**	Milliliters
MO-MDSCs	**:**	Monocytic Myeloid-Derived Suppressor Cells
ms	**:**	Months

MΦ	**:**	Macrophage
NOS	**:**	Nitric Oxide Synthase 2
PBMCs	**:**	Peripheral Blood Mononuclear Cells
PBS	**:**	Phosphate Buffered Saline
PD-L1	**:**	Programmed Death-Ligand 1
PTPN22	**:**	Protein Tyrosine Phosphate Non receptor type22
RA	**:**	Rheumatoid Arthritis
RhIG	**:**	Rh_oD Immune Globulin
ROS	**:**	Reactive Oxygen Species
SLE	**:**	Systemic Lupus Erythematosus
TCR	**:**	T-cell Receptor
T1D	**:**	Type 1 Diabetes mellitus
Th1	**:**	T helper 1
Th2	**:**	T helper 2
TGF-β	**:**	Transforming Growth Factor - beta
TLC	**:**	Total Leukocytic Count
TNF-α	**:**	Tumor Necrosis Factor - alpha
TPO-R	**:**	Thrombopoietin Receptor
TPO-RA	**:**	Thrombopoietin Receptor Agonist
Tregs	**:**	Regulatory T cells
USA	**:**	United States of America

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Abstract

Background: Regulatory T cells have an immunosuppressive function on T cell activation. They are involved in pathophysiology and treatment of immune thrombocytopenia (ITP). Circulating myeloid–derived suppressor cells (cMDSCs) are involved in immune dysregulation in ITP. **Study objective** was to determine the mean level of MDSCs in acute, persistent and chronic ITP, and its impact on treatment modalities and prognosis. **Patients and Methods:** Forty-one patients with ITP were recruited from Pediatric hematology clinic, Ain Shams University. They were classified into acute, persistent and chronic. they were compared to 20 age and gender matched as healthy controls. All patients were subjected to history taking with emphasis on age of presentation, disease duration and treatment modalities, thorough clinical examination. Mean values of CRP, ALT, S. Creatinine were collected from patients' files. All study participants have performed CBC (Coulter), MDSCs by flow cytometry. Secondary thrombocytopenia was excluded. **Results:** Acute ITP was detected in 29%, 24% had persistent and 46% had chronic ITP. Their age ranged from 1- 16 years at study entry, 51.2% were male. Active disease was found in 58.5% while 41.4% in remission. No treatment was offered to 53% while 24% of patients were on steroids. MDSCs decreased significantly in ITP patients Vs control group ($P < 0.001$) while didn't show significant difference among patients' group regarding MDSCs level as P value =0.325 or with different treatment modalities. **Conclusion:** Reduced numbers of MDSCs play a role in pathogenesis of ITP. Yet, MDSCs didn't differ according to disease duration or treatment modalities.

Keywords: Immune Thrombocytopenia, Pediatric, T lymphocyte, MDSC