

Study of IL4 in Acute and Chronic ITP in Pediatric Patients

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

سورة البقرة الآية: ٣٢



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Candidate

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List of Contents

<i>Subject</i>	<i>PageNo.</i>
List of Abbreviations.....	i
List of Tables.....	iii
List of Figures	v
Abstract	vi
Protocol.....	
Aim of the Study	1
Review of Literature	
Immune Thrombocytopenia (ITP)	2
Interleukin-4	31
The Role of Cytokines in the Pathogenesis of ITP	43
Subjects and Methods	50
Results.....	60
Discussion	76
Summary	82
Recommendations	85
References	86
Appendix	I
Arabic Summary	—

List of Abbreviations

<i>Abbr.</i>	<i>Full-term</i>
ACTH	: Adrenocorticotrophic hormone
AD	: Atopic dermatitis
ADO	: Adenosine
Ag	: Antigen
APC	: Antigen presenting cells
ASH	: American society of heamatology
CGRP	: Calcitonin gene related peptide
cITP	: Chronic ITP
CR	: Complete response
CRH	: Corticotropin releasing hormone
DAT	: Direct antiglobulin test
DC	: Dendritic cell
ELISA	: Enzyme–linked immunosorbent assays
EMBP	: Eosinophilic major basic protein
HPAA	: Hypothalamic pituitary adrenal axis
IFN	: Interferon
IL	: Interleukin
IQR	: Interquartile range
ITP	: Immune thrombocytopenic purpura
IVIg	: Intravenous immunoglobulin
IWG	: International Working Group

List of Abbreviations *(Cont.)*

<i>Abbr.</i>	<i>Full-term</i>
NE	: Norepinephrine
NK	: Natural killer cells
PaIgG	: Platelet associated IgG
PBQ	: Pediatric bleeding questionnaire
RBCs	: Red blood cells
ROC	: Receiver operating characteristic
SD	: Standard deviation
SNS	: Sympathetic nervous system
SP	: Substance P
Tc	: T-cytotoxic
TCR	: T cell's receptor
TGF	: Transforming growth factor
Th	: T-helper
TNF	: Tumor necrosis factor
TPO	: Thrombopoietin
WBCs	: White blood cells

List of Tables

<i>Table No.</i>	<i>Title</i>	<i>Page No.</i>
Table (1):	Classification of the severity of bleeding.....	16
Table (2):	Frequent examples of differential diagnosis of ITP and potential alternative causes of thrombocytopenia identified by patient history.....	19
Table (3):	First-line/initial treatment in children with ITP.	22
Table (4):	The scoring key for the Pediatric Bleeding Questionnaire.....	52
Table (5):	Number and percentage of the groups.....	60
Table (6):	Statistical comparison between groups regarding demographic data	61
Table (7):	Statistical comparison between groups regarding bleeding score.....	65
Table (8):	CBC parameters in acute and chronic ITP patients.....	66
Table (9):	Comparison between acute and chronic ITP patients regarding anemia, lymphopenia and neutropenia.....	68
Table (10):	Comparison between acute and chronic ITP patients regarding treatment received.....	69
Table (11):	Comparison between groups regarding level of IL4	70
Table (12):	Comparison between level of IL4 in the different treatment groups of acute patients. ...	71

List of Tables *(Cont.)*

<i>Table No.</i>	<i>Title</i>	<i>Page No.</i>
Table (13):	Comparison between level of IL4 in different treatment groups of chronic patients.....	72
Table (14):	Correlation between level of IL4 and all items in chronic patients	75

List of Figures

<i>Figure No.</i>	<i>Title</i>	<i>Page No.</i>
Figure (1):	Pathogenic mechanisms in ITP	8
Figure (2):	Schematic of shifts in the T-cell balance in ITP	12
Figure (3):	Summary of the complex mechanism of antiplatelet activity in patients with ITP.....	12
Figure (4):	Mechanisms of action of therapies for immune thrombocytopenic purpura	26
Figure (5):	IL-4 receptor complexes.....	36
Figure (6):	A simplified scheme of the bidirectional communication between the brain in the immune system.....	45
Figure (7):	Schematic of shifts in the T-cell balance in ITP	47
Figure (8):	Standard curve for human IL-4 concentration	56
Figure (9):	Example of IL-4 concentration in an acute patient	57
Figure (10):	Example of IL-4 concentration in a chronic patient	58
Figure (11):	Number and percentage of the groups.....	60
Figure (12):	Comparison between groups regarding sex.....	63
Figure (13):	Percentage of males and females in acute and chronic ITP groups.	63

List of Figures (Cont.)

<i>Figure No.</i>	<i>Title</i>	<i>Page No.</i>
Figure (14):	Comparison between groups regarding age.....	64
Figure (15):	Comparison between groups regarding bleeding score	65
Figure (16):	Comparison between acute and chronic ITP groups regarding CBC parameters.	67
Figure (17):	Comparison between acute and chronic ITP patients regarding anemia, lymphopenia and neutropenia.....	68
Figure (18):	Comparison between groups regarding treatment received.....	69
Figure (19):	Comparison between groups regarding level of IL4	70
Figure (20):	Comparison between level of IL4 in acute patients who received treatment and those who didn't receive.....	71
Figure (21):	Comparison between level of IL4 in chronic patients who received treatment and those who didn't receive	72
Figure (22):	Negative correlation between Level of IL-4 and age.....	74
Figure (23):	Negative correlation between Level of IL-4 and weight.....	74
Figure (24):	Positive correlation between level of IL4 and lymphocytic count in chronic patients....	75

ABSTRACT

Background: Immune thrombocytopenia (ITP) is an autoimmune disease where platelets are destroyed prematurely. In the majority of children the disease resolves, but in some it becomes chronic. IL-4 is also termed B cell stimulatory factor 1 and is involved in B-cell activation and antibody production but also in T-cell activation. IL-4 is also known for its role in Th2 response **Aim of the Work:** This study was designed to compare IL4, bleeding score and lymphocytic count between acute and chronic ITP patient. **Subjects and methods:** The serum level of IL4 was assessed by ELISA in 20 newly diagnosed and 15 chronic ITP pediatric patients; we also compared bleeding score and lymphocytic count between both groups. **Results:** In this study IL4 differ significantly between newly diagnosed and chronic ITP patients with higher levels among newly diagnosed patients. However, there was no difference between both groups regarding bleeding score or lymphocytic count. **Conclusion:** Our data indicate that cytokine disturbances especially IL4 might be involved in the pathogenesis of newly diagnosed ITP.

Key words: Immune thrombocytopenia, Interleukin-4, bleeding score

Introduction

Immune thrombocytopenic purpura (ITP) is a heterogeneous clinical disorder characterized by immune-mediated platelet destruction. ITP is usually a benign, self-limiting disease in children (*Provan et al., 2010*).

However, approximately 20% of childhood newly diagnosed ITP progress to a chronic form defined according to standardized criteria (*Rodeghiero et al., 2009*).

Primary ITP was previously split into acute and chronic ITP depending on the outcome, however, the condition is today divided into 3 phases depending on the duration of thrombocytopenia after the initial diagnosis, that is newly diagnosed up to 3 months persistent ITP between 3 and 12 months, and chronic ITP beyond 12 months (*Rodeghiero et al. 2009*).

The clinical differences between newly diagnosed and chronic ITP suggest the existence of different pathophysiological mechanisms in the two forms (*Stasi et al., 2008*).

Many researchers have investigated the role of genetic factors, humoral and cellular immunity, and inadequate platelet production in the development of this condition, but failed to identify specific characteristics of children with ITP who will probably develop the chronic form of the disorder,

mainly because of the study design and differences in patients' immunomodulating therapy (*Nugent et al., 2009*).

Clinical findings indicate that the development of chronic ITP in children is associated with older age, less mucosal bleedings, and an insidious onset. Furthermore, chronic ITP is less likely to have had a viral illness before onset and has higher platelet count at presentation than in children with a spontaneously resolving ITP (*Glanz et al. 2008*).

At presentation there are no clinical useful biomarkers that can separate a spontaneously resolving disease from the chronic variant (*Jernas et al., 2013*).

Nevertheless, *Semple et al. (1996)* found increased serum levels of interleukin 2 (IL-2), IL-10, and interferon- γ in chronic ITP compared with acute ITP. *Del Vecchio et al. (2012)* also found increased serum levels of IL-10 in chronic versus acute ITP.

Recently *Jernas et al. (2013)* found increased levels of interleukin (IL) 16 and TNF – related weak inducer of apoptosis and lower levels of IL4 in newly diagnosed Compared with chronic ITP.

IL-4 is also termed B cell stimulatory factor 1 and is, as the name implies, involved in B-cell activation and antibody production but also in T-cell activation. IL-4 is also known for its role in Th2 response (*Yakura et al., 1988*).

Aim of the Study

The aim of this study is to compare bleeding score and lymphocytic index between acute and chronic ITP patients, we will also measure level of IL4 in both groups to assess if there is a pathophysiologic difference between both disease processes. This may help to find tools to predict disease progression.