Ain Shams University
Faculty of postgraduate childhood studies

# Prognostic Clinical and Laboratory Parameters in Children with primary Immune Thrombocytopenic Purpura

Thesis

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# List of Abbreviations

| | |
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| **AIEOP** | Associazione Italiana di Ematologia e Oncologia Pediatrica |
| **ALC** | Absolute lymphocyte count |
| **ALPS** | Autoimmune lymphoproliferative syndrome |
| **ANA** | Anti-nuclear antibody |
| **ANOVA** | Analysis of variance |
| **Bregs** | Regulatory B cells |
| **CagA** | Cytotoxin associated gene A |
| **CBC** | Complete Blood Count |
| **CVID** | Common variable immunodeficiency |
| **DTap** | Diphtheria Tetanus Pertussis Vaccine |
| **EDTA** | Ethylenediaminetetraacetic acid |
| **ELISA** | Enzyme Linked Immunosorbent Assay |
| **FCIA** | Flow Cytometric Immunobead assay |
| **Hb** | Hemoglobin |
| **HCV** | Hepatitis C virus |
| **HIV** | Human immunodeficiency virus |
| **ICIS** | Intercontinental cooperative ITP study group |

| | |
|---|---|
| **ITAMs** | Immunoreceptor tyrosine-based activation motifs |
| **ITIM** | Immunoreceptor tyrosine-based inhibitory motif |
| **ITP** | Immune thrombocytopenia |
| **IVIG** | Intravenous immunoglobulin |
| **IWG** | International Working Group |
| **JAK** | Janus kinase |
| **KIR** | Killer cell immunoglobulin-like receptor |
| **LS** | Laparoscopic splenectomy |
| **MAP** | Mitogen-activated protein |
| **MMR** | Measles Mumps Rubella Vaccine |
| **MPV** | Mean platelet volume |
| **OD** | Optical densit |
| **PARC-ITP** | Pediatric and Adult Registry of Chronic ITP |
| **RAISE** | Randomized Placebo- Controlled ITP Study with Eltrombopag |
| **RITP** | Refractory idiopathic thrombocytopenic purpura |
| **RPM** | Revolutions  per minute |
| **SDMP** | Standard-Dose Methylprednisolone |

| | |
|---|---|
| **SPSS** | Statistical package for social science |
| **STAT** | Signal transducers and activators of transcription |
| **TLC** | Total leukocyte count |
| **Tregs** | Regulatory T cells |
| **WASP** | Wiskott-Aldrich syndrome protein |
| **WBCs** | White blood cell |

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# INTRODUCTION

The term ITP refers to “immune thrombocytopenic purpura,” “idiopathic thrombocytopenic purpura,” and, most recently, “immune thrombocytopenia” ***(Ruggeri et al., 2008)***.

ITP is an autoimmune disease characterized by a decreased platelet count ( less than $100 \times 10^9$/L) due to destruction of antibody-sensitized platelets in the reticuloendothelial system (RES) ***(Blanchette and Bolton-Maggs, 2010, Lanzkowsky, 2011)*.**

Primary ITP is isolated thrombocytopenia (platelet count < $100 \times 10^9$/L) in the absence of disorders or other causes that may be presented with thrombocytopenia ***(Semple et al., 2010)*.**

Secondary ITP is any form of immune disease causing thrombocytopenia except primary; such as systemic lupus erythematosus (SLE), infection with hepatitis C or lymphoproliferative disease ***(Lanzkowsky, 2011)*.**

The term “newly-diagnosed ITP” now replaces the old term “acute ITP”, which is any ITP diagnosed within the preceding 3 months. Persistent ITP refers to immune thrombocytopenia of 3-12 months duration, while immune thrombocytopenia more than 12 months duration is refer to chronic ITP ***(Semple et al., 2010, Lanzkowsky, 2011)*.**

Primary ITP is a diagnosis of exclusion by carefully ruling out causes of pseudo thrombocytopenia, secondary ITP, and inherited ITP. Obtaining an accurate history combined with a complete blood count is the first and most important step. The diagnosis of ITP is based up on the following criteria:

- Acute onset of bruising and petechiae in an otherwise healthy child-often with a recent history of viral infection.
- Platelet count <100,000×$10^9$/L (often <20,000×$10^9$/L).
- Otherwise normal complete blood count (CBC) with differential white count, and reticulocyte count.
- No abnormalities on the peripheral blood smear after review by an experienced practitioner. In particular, there should be no evidence of hemolysis or of blast cells.
- No clinically apparent associated conditions that may cause thrombocytopenia, after a thorough history and physical examination. Findings that suggest a diagnosis other than ITP include enlargement of lymph nodes, liver, spleen or systemic symptoms (e.g., fever, anorexia, bone or joint pain, or weight loss) ***(Rodeghiero et al., 2009).***

The majority of children with acute ITP will require only advice, support and repeat CBC 10 days after diagnosis to ensure that there is no generalized marrow disorder. Further monitoring of the CBC is not required unless a change in the child's condition takes place to suggest that remission has occurred, or that deterioration has taken place.

Any of the following may be used in a special setting if it is thought that the clinical condition requires that the platelet count should be raised :( prednisone, intravenous immunoglobulin, IV anti-D immunoglobulin).

The majority of children achieve spontaneous remission and do not suffer major bleeding complications despite a platelet count <10 × $10^9$/L.

The expectant 'watch and wait' policy of management is recommended for such patients. In the absence of 'wet bleeding', the child does not require hospitalization. The frequency of follow up blood counts should be limited to every 1-2 weeks initially and lesser thereafter, in order to avoid unnecessary hospital visits and anxiety ***(Imbach et al., 2006).***

Anti-D may be considered for first-line therapy in Rh + non splenectomized children ***(Neunert et al., 2011).***

## Definition of study concepts:

**ITP**: it is an autoimmune disorder characterized by immunologic destruction of otherwise normal platelets most commonly occurring in response to an unknown stimulus.

**Primary ITP**: is a platelet count less than 100 x $10^9$/L in the absence of other causes or disorders that may be associated with thrombocytopenia.

**Mean platelet volume (MPV):** is a measure of platelet size.

**A viral prodroma**: is defined as a documented history of upper respiratory tract illness (URI), gastrointestinal (GI) symptoms, or skin exanthema within 4 weeks of diagnosis of ITP.

**Pseudo thrombocytopenia**: is the result of platelets clumping in the presence of ethylenediaminetetraacetic acid (EDTA).