# Detection of Primary Immunodeficiency in Children with Recurrent Infection

*Thesis*

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# تحديد أمراض نقص المناعة الأولية في الأطفال المصابين بالالتهابات الميكروبية المتكررة

رسالة

توطئة للحصول على درجة الماجستير في طب الأطفال

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# List of Abbreviations

| | |
|---|---|
| **AAAAI** | American Academy of Allergy Asthma and Immunology |
| **Ab** | Antibody |
| **AD** | Autosomal dominant inheritance |
| **ADA** | Adenosine deaminase |
| **AEC** | Absolute Eosinophilic count |
| **ALC** | Absolute lymphocytic count |
| **ANA** | Absolute neutrophilic count |
| **APC** | Antigen presenting cells |
| **AT** | Ataxia telangiectasia |
| **BMT** | Bone marrow transplantation |
| **CBC** | Complete blood count |
| **CGD** | Chronic granulomatous disease |
| **CID** | Combined immunodeficiency |
| **CMV** | Cytomegalovirus |
| **CRP** | C-Reactive protein |
| **CTL** | Cytotoxic T- lymphocyte |
| **CVID** | Common variable immunodeficiency |
| **DGS** | DiGeorge syndrome |
| **DHR** | Dihydrorhodamine |
| **DTH** | Delayed-type hypersensitivity |
| **FCM** | Flow cytometry |
| **FITC** | Fluorescein isothiocyanate |
| **Hb** | Haemoglobin |
| **HC** | Hemolytic complement |

| | |
|---|---|
| **HIM** | Hyper-IgM syndrome |
| **HIV** | Human immunodeficiency virus |
| **HSCT** | Hematopoietic stem cell transplantation |
| **Ig** | Immunoglobulin |
| **IgA** | Immunoglobulin A |
| **IgD** | Immunoglobulin D |
| **IgE** | Immunoglobulin E |
| **IgG** | ImmunoglobulinG |
| **IgM** | Immunoglobulin M |
| **IL** | Interleukin |
| **IPEX** | Immunodysregulation, polyendocrinopathy, enteropathy, X-linked syndrome |
| **IQR** | Interquartable range |
| **IVIG** | Intravenous immunoglobulin |
| **L** | Lymphocyte |
| **LAD** | Leucocyte adhesion defect |
| **MHC** | Major Histocompatibility |
| **NEMO** | Nuclear factor kB essential modulator, also called IKK-g |
| **NK** | Natural killer |
| **PCP** | Pneumocystis carinii pneumonia |
| **PE** | Phycoerythrine |
| **PID** | Primary immunodeficiency disease |
| **RBCs** | Red blood cells |
| **SCID** | Severe combined immunodeficiency |
| **SCIG** | Subcutaneous immunoglobulin |
| **Sig.** | Significance |
| **TCR** | T-cell receptor |

| | |
|---|---|
| **TH** | T-helper cell |
| **TLC** | Total leucocytic count |
| **TLR3** | Toll-like receptor |
| **TNF** | Tumor necrosis factor |
| **Treg** | T-regulatory cell |
| **TRECs** | T-cell receptor excision circles |
| **WAS** | Wiskott Aldrich syndrome |
| **XLA** | X-linked agammaglobulinemia |
| **XLP** | X-linked lymphoproliferative syndrome |

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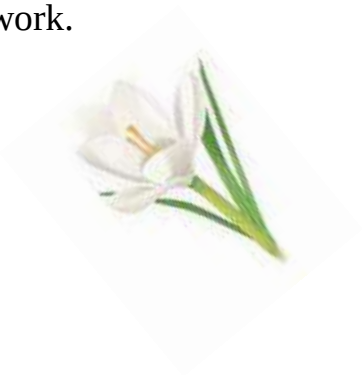


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# Introduction

Primary immunodeficiency diseases (PID) represent a class of disorders in which there is an intrinsic defect in the human immune system (rather than immune disorders that are secondary to infection, chemotherapy or some other external agent). In some cases, the body fails to produce any or enough antibodies to fight infection. In other cases, the cellular defenses against infection fail to work properly. There are more than 150 different PID currently recognized by the World Health Organization **(Boyle and Buckley, 2007).**

PIDs can affect components of the adaptive immune system, namely T cells and B cells, as well as components of the innate immune system, namely neutrophils, phagocytes, complement, and natural killer cells **(Notarangelo et al., 2006)**.

The principal clinical manifestation of immunodeficiency is increased susceptibility to infection. The pattern of organ systems affected and characteristic pathogen vary with the type of immune defects. Therefore, it is important to look for primary immunodeficiency in any infant or child with recurrent infections **(Chaple, 2005).**

The reason for missing the diagnosis may be many and include: low index of suspicion, very high rates of infections in the general population and non-availability of diagnostic facilities at most centers **(Verma et al., 2008).**

# Aim of the Work

The purpose of this study is to evaluate the lymphocyte subsets among infants and children with recurrent infection, especially among those with lymphopenia in order to recognize patients with primary immunodeficiency diseases.

# Primary Immunodeficiency Diseases

## Definitions:

Primary immunodeficiencies (PIDs) are heritable disorders of immune system function. Many are associated with single gene defects, whereas others may be polygenic or may represent interaction of genetically determined characteristics with environmental or infectious stresses **(Bonilla and Geha, 2005).**

PIDs are a group of genetically diverse diseases which affect distinct components of innate and acquired immunity, including the development and function of complement proteins, dendritic cells, granulocytes, natural killer cells, T and B lymphocytes **(Geha et al., 2007).**

## Epidemiology:

Ten percent of children with recurrent infections have an immunodeficiency, with a defect in one or more components of the immune system. Components of the adaptive immune system include B cells (humoral or antibody system) and T cells (cellular system). The innate immune system is made up mainly of the phagocytic cell system and the complement system **(Bonilla et al., 2005)**.

Almost three-fourths of the primary immunodeficiencies are caused by an antibody (B cell) deficiency or a combined B and T cell abnormality. Isolated T cell defects, as well as phagocytic cell, complement, and other innate immune defects, are much less common. Thus, B cell (antibody) or combined B and T cell diseases should be considered initially, unless clinical features suggest otherwise **(Stiehm et al., 2004)**.

# Classifications of PIDs:

PID disorders are classified into 8 main groups based on syndromes, diseases of immune dysregulation & the type of cells affected **(Notarangelo et al., 2009)**. These groups are combined B and T-cells immuno-deficiencies, predominantly antibody deficiencies, other well defined immunodeficiency defect of phagocyte (number, function, or both), defects in innate immunity, autoinflammatory disorders, and complement deficiencies. Associated features and mode of inheritance of PID disorders of these groups are presented in (table1).