

Primary Immunodeficiency in Children: Report of Seven Years Study

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ABSTRACT

Background: Primary immunodeficiency diseases (PIDs) are a genetically heterogeneous group of disorders that affect distinct components of the innate and adaptive immune system, such as neutrophils, macrophages, dendritic cells, complement proteins, natural killer cells, T and B lymphocytes. These disorders are rare, with an estimated prevalence of 1:10,000 live births.

Objectives: This study aimed at describing the clinical features, disease complications, treatment modalities and overall outcome of patients with Primary Immunodeficiency Diseases (PID) in Masih Daneshvari hospital during a 7-year period (2001-2008).

Materials and Methods: This was a retrospective study based on the review of patients' medical records. Clinical, laboratory, and epidemiological data including personal and family history were obtained by reviewing records of patients admitted to the Pediatric Pulmonary Ward of NRITLD, a referral center for tuberculosis and lung diseases. The diagnosis was made based on WHO criteria for primary immunodeficiency disorders.

Results: Data collected from 59 patients were evaluated and analyzed. There were 35 (59.3%) males and 24 (40.69%) females. The age of patients ranged from 6 months to 14.5 years and the mean age was 7.4 years. Positive family history was detected in 20 (33.9%) cases and parents of 36 patients (61.2%) were consanguineous. Twenty patients (33.9%) had a family history of PID. Phagocytic disorder (57.2%) was the most common form of PID, followed by antibody deficiency (33.7%) and T-cell or combined deficiency (8.2%). No case of complement deficiency was detected. In this group of under study patients, 2 cases expired as the result of respiratory failure due to drug resistant pneumonia (chronic granulomatous disease cases).

Conclusion: Based on studied results, Phagocytic disorders (57.2%) were the most common disorders among our PID patients. This may be due to the large number of CGD patients referred with the pathologic finding of granuloma misdiagnosed with tuberculosis. Considering the high prevalence of PID in this study, cases with unusual, chronic, severe or recurrent infections should be evaluated for immunodeficiency disorders. (*Tanaffos*2011; 10(2): 38-43)

Key words: Primary immunodeficiency disorders, Cellular immunity, Humoral immunity, Phagocytic disorders, Children

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INTRODUCTION

Primary immunodeficiency diseases (PIDs) are a genetically heterogeneous group of disorders that affect distinct components of the innate and adaptive immune system, such as neutrophils, macrophages, dendritic cells, complement proteins, natural killer cells, and T and B lymphocytes. Most primary immunodeficiencies are genetic disorders; the majority are diagnosed in children under the age of one, although milder forms may not be recognized until adulthood (1,2).

Extensive use of antibiotics by physicians has masked the classic presentation of many of the primary immunodeficiency diseases. Evaluation of immune function should be initiated for children with clinical manifestations for a specific immune disorder or with unusual, chronic, or recurrent infections such as systemic bacterial infections, serious respiratory bacterial infections, liver or brain abscess, infection with unusual pathogens and infections with common childhood pathogens but of unusual severity (3).

These disorders are rare, with a prevalence of 1:10,000 live births (3). A generally accepted classification of PID includes: antibody deficiency, cellular deficiency, combined (humoral and cellular) immunodeficiency, phagocytic disorders, and complement deficiency. More than 100 different types of PID have been recognized (4-8)

Reports on PID prevalence are available from different countries and show wide geographical and racial variations in prevalence.

The purpose of our study was to enhance the knowledge of physicians about PID and to determine the frequency of these disorders in children admitted to the Pediatric Pulmonary Ward of National Research Institute of Tuberculosis and Lung diseases. We retrospectively analyzed the charts of 59 children who were diagnosed and treated for PID in a 7-year period (2001-2008) (9).

MATERIALS AND METHODS

This retrospective descriptive study was conducted during a 7-year period (2000-2007) in the pediatric ward of Masih Daneshvari Hospital. The Medical files of all patients admitted to the ward with the diagnosis of primary immunodeficiency disorder during the mentioned period were evaluated in this research. Data were recorded in a questionnaire prepared especially for this purpose.

Diagnostic criteria for this disorder were similar to WHO based criteria. All Patients aged 18 or younger entered the study. Information regarding demographic data (including age, sex, height/weight, consanguinity of parents and family history of any immunologic disorders), laboratory examinations (NBT level, Igs, complement level, flow-cytometry, gastric washing for AFB, sputum smear and PPD), clinical manifestations, radiologic features and the type of PID were obtained from the medical files and analyzed using SPSS software.

PPD test results were divided into 4 groups of 0-5 mm, 6-10 mm, 11-15 mm and >15 mm. PPD >15mm was considered as positive. NBT (Nitro blue tetrazolium test) was classified into 3 groups of 0-10%, 15-90% and 90-100%. A test result of 0-10% was regarded as abnormal.

RESULTS

In this evaluation, medical files of 59 patients were studied. There were 35 (59%) male and 24 (41%) female patients. The age of patients ranged between 1 month to 14.5 years; with a mean age of 7.4 years.

Positive family history was observed in 20 (33.9%) cases and parents of 36 children (61.2%) had consanguinity.

Growth curve was below 5% percentile in 41 children (69.4%), between 5%-25% in 8 (13.5%) cases, between 25%-50% in 5 (8.4%) and more than 50% percentile in another 5 patients.

Clinical manifestations are shown in Figure 1.

The most common complaints were dry cough (in 53 cases, 89.8%), fever (in 36 cases, 61%), productive cough (in 19 cases, 32.2%) and recurrent GI infections (in 6 cases, 10.1%).

Chest and abdominal findings based on radiological evaluation are demonstrated in Figures 2 and 3, respectively.

NBT in 5 CGD patients (3 boys, 2 girls) was below 5%. PPD was positive in 6, all of whom were diagnosed as CGD patients. The most prevalent disorders were phagocytic abnormalities (in 34 cases, 57.2%), antibody deficiency (in 20 cases, 33.7%) and T-cell or combined deficiency cases (8.2%). There were no cases of complement system deficiency (Table 1).

Table 1. Summary of the PID patients

Category	No (%)	Male	Female	Age	Mortality	Family history of immunologic disorders
Antibody deficiency	20 (34)	15	5	6/5	0	6 (30%)
Common variable Immunodeficiency	15 (25/4)	10	5	5/3	0	4 (27%)
Selective IgA deficiency	2 (3/3)	1	1	4/5	0	1 (50%)
Bruton	3 (5)	3	0	9/8	0	1 (20%)
T-cell or combined immunodeficiency	5 (8/2)	1	4	7/9	0	1 (20%)
Ataxia telangiectasia	1 (1/6)	0	1	14/7	0	0
Severe combined immunodeficiency (SCID)	1 (1/6)	1	0	<1	0	1
Autoimmune lymphoproliferative syndrome (ALPS)	3 (5)	0	3	8/3	0	0
Phagocytic defects	34 (58)	20	14	4/8	2	13 (38%)
Chronic granulomatous disease	20 (33/9)	13	7	8/4	2	10
IFN-gamma deficiency	2 (3/3)	2	0	4	0	0
IL-12 deficiency	5 (8/4)	3	2	5/4	0	1
Hyper IgE syndrome	5 (8/4)	0	5	8/1	0	1
Cyclic neutropenia	1 (1/6)	1	0	<1	0	0
Leukocyte adhesion deficiency (LAD)	1 (1/6)	1	0	2	0	1
Complement deficiency	0 (0)					

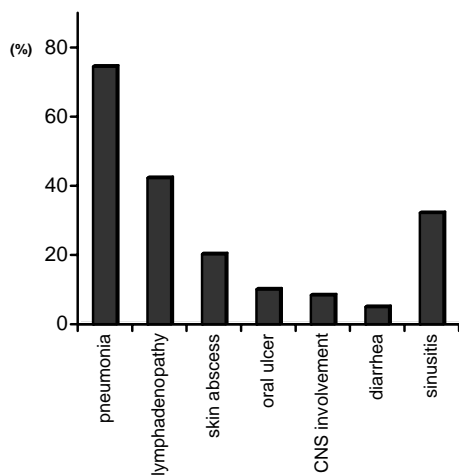


Figure 1. Clinical manifestations in patients.

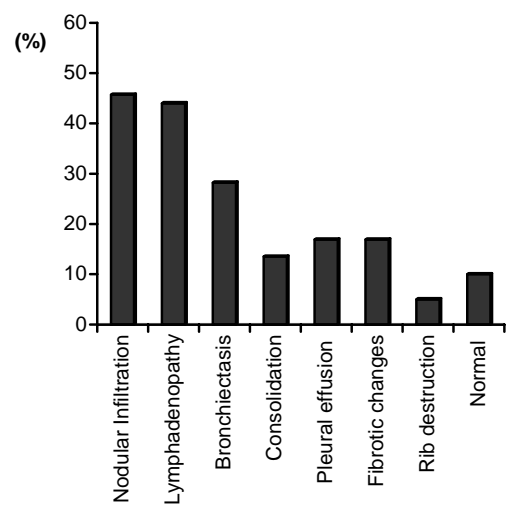


Figure 2. Result of chest CT scan in patients.

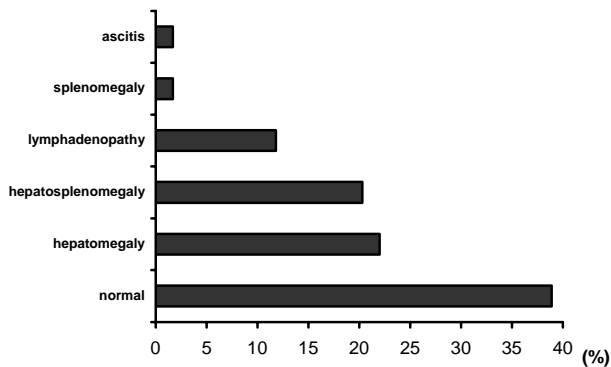


Figure 3. Abdominal CT-scan findings.

DISCUSSION

In the current study the etiology and frequency of PID in 59 admitted children was evaluated. In a similar study performed by Farhoudi and colleagues in one of the university hospitals of Tehran during a 20-year period, 247 cases of PID were identified among children (53.3% - 130 cases) and adults. However, there are no exact data on the rate of PID among Iranian children (7).

In another study conducted in 2002 in Israel, 11 hospitals were studied over a 7-year period and 249 cases of PID were reported (4).

Golan et al. study conducted in 2002 showed a boy / girl ratio of 2/1. In our research this ratio was 4/1. The high rate of occurrence in boys could be explained by the x-linked diseases such as CGD, Wiskott-aldrich, hyper IgM and SCID (4).

The notable point is that the number of PID patients in this research does not reflect the actual prevalence of this disease. In other words, many patients with serious forms of immunodeficiency such as SCID expire in infancy and early childhood and remain unknown (10-12).

Some with mild forms of the disorder, IgA deficiency and other subclass deficiencies are treated by the physicians and thus are not referred to any referral center.

Infection is the chief complaint in PID cases. All

types of infections can occur; however, recurrent and chronic respiratory infections are the most common presenting features. Other forms of infection such as diarrhea, abscess, septic arthritis, sepsis and meningitis are also present. The present study demonstrated respiratory, cutaneous and GI infections as the most prevalent forms of infection (13,14).

In the current study, we found positive family history in 33.9% of PIDs with phagocytic defects.

In a study conducted in Taiwan in 2005, antibody deficiency (46%), T-cell or combined deficiency (30%) and phagocytic disorders (24%) were the most prevalent abnormalities reported and there were no cases of complement deficiency (15).

In 2006, a similar study was performed on 930 patients registered in the Iranian PID registry. According to this research the most common defects were antibody deficiency (38.4%), defect in phagocytic system (28.3%), T-cell or combined deficiency (11%), complement system defects (2.4%), other immune system disorders (17.7%) and immune dysregulation disease (2.3%) (9).

Based on our results, phagocytic disorders (57.2%) were the most common disorders in PID children who had referred to our center. This was followed by antibody deficiency (33.7%) and T-cell or combined deficiency (8.2%).

Overall prevalence of complement system deficiency is very small, in other countries this rate is about 2-7% (16,17,18,19,20,21,22)

This difference could be due to the fact that our center is a referral center for TB and lung diseases. Therefore, it could be the reason for the greater incidence and bias noticed in the study of CGD patients that were admitted due to respiratory infections and pathologic findings of granulomatous lesions misdiagnosed as tuberculosis.

In case of eliminating the mentioned referred

cases, our results will be similar to those of other countries and the most common defect observed would be antibody deficiency.

Among the antibody deficiency disorders, CVID (75%) was the most prevalent defect, a finding similar to that of studies conducted in Spain, Sweden and Iran (9, 17, 20).

According to certain reports, the most common phenotype of PID is IgA deficiency; European studies report its prevalence to be 33-50%.

However, in our study there were only 2 cases of IgA deficiency (3.39%). This rate was similar to that of other studies performed in Australia, Japan and Iran (7, 16, 21).

As compared to other researches, SCID cases were fewer in number which could be due to the high mortality of these patients at a very young age (10,11,12,16, 18, 23).

Finally based on the results of this study and reports from other parts of the country, it seems that actual rate of PID in Iran is much higher than the rate reported. Also, in cases with recurrent episodes of systemic infections or infection with an unusual organism, evaluation of the immunologic system is highly recommended.

Early diagnosis and treatment of PID are especially important in decreasing the incidence of infections, complications and hospitalization of PID patients.

An increase in knowledge for detection of primary immunodeficiency disorders is important, not only for earlier diagnosis but also for better treatment of patients and diminishing possible complications more effectively.

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