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Primary Immunodeficiency in Iran: First Report of the National Registry of PID in Children and Adults

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Epidemiological studies have shown wide geographical and racial variation in the prevalence and patterns of immunodeficiency disorders. To determine the frequency of primary immunodeficiencies (PID) in Iran, the Iranian Primary Immunodeficiency Registry (IPIDR) was organized in 1999. We extracted the patient's data, by using a uniform questionnaire from their hospital records. The diagnosis of patients was based on WHO criteria. By now, 440 patients with PID, who were observed during a period of 20 years, have been registered in our registry. Among these patients, the following frequencies were found: predominantly antibody deficiency in 45.9% of patients (n = 202), phagocytic disorders in 29.09% (n = 128), T-cell disorders in 24.31% (n = 107), and complement deficiencies in 0.68% (n = 3). Common variable immunodeficiency was the most frequent disorder (n = 98), followed by chronic granulomatous disease (n = 86), ataxia telangiectasia (n = 48), x-linked agammaglobulinemia (n = 45), selective IgA deficiency (n = 42), combined immunodeficiency (n = 15), and severe combined immunodeficiency (n = 14). This study revealed that antibody deficiencies is the most frequently diagnosed primary immunodeficiency disorder in our patients, which is similar to that observed in other registries. A comparative study shows some differences between our results and other registries.

KEY WORDS: Primary immunodeficiency; National registry; Iran.

INTRODUCTION

Primary immunodeficiencies (PID) are a group of disorders characterized by an unusual susceptibility to infections. Since Bruton's first description of agammaglobulinemia in 1952 (1), about 80 different primary immunodeficiency disorders have been recognized (2). This increase in the recognition rate of more different types of primary immunodeficiency disorders is due to advances in our knowledge about the immune system and the novel progress in immunological and molecular techniques. Estimated occurrence of primary immunodeficiencies is about 1 per 10,000 live births (excluding asymptomatic IgA deficiency) (3). Epidemiological studies have shown wide geographical and racial variations in the prevalence and the pattern of immunodeficiency diseases. Physicians and general practitioners are often poorly informed about the clinical presentation, diagnostic approach, importance, and health impact of primary immunodeficiencies; thus, some patients may remain untreated for several years and this will lead to many complications for them (4–7).

In order to discover the frequency of the different forms of primary immunodeficiency, we organized the

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Iranian Primary ImmunoDeficiency Registry (IPIDR) in 1999. Our goal was to enhance the knowledge about these diseases among general practitioners and pediatricians, to emphasize the importance of early diagnosis and treatment, to determine the frequency of these diseases in Iran, to stress the importance of teaching the clinical immunology in the medical curriculum, and finally to promote research about primary immunodeficiencies in our country.

This article provides data on Iranian patients with primary immunodeficiency diseases, classified according to WHO criteria (2) and diagnosed between 1981 and 2001.

PATIENTS AND METHODS

Registry Questionnaire

A four-page questionnaire was developed to contain all the patient's demographic information, including name, date of birth, place of birth, the diagnosis of PID, first clinical presentation, age at the time of onset of symptoms, age at the time of diagnosis of the PID, family history of immunodeficiency and/or recurrent infections, family history of autoimmune diseases and malignancies, basic immunological laboratory tests, follow-up information including the infections in the course of the illness and name of the immunologist, and who has referred the patient's information to IPIDR center. This questionnaire was sent to the universities participating in IPIDR.

Participating Centers

This initial survey, which included patients diagnosed from 1981 onward, covered seven universities of medical sciences from five major states of Iran, including Tehran, Shiraz, Mashhad, Isfahan, and Babol. The explanation for selecting these universities as a participant of this registry was the existence of immunodeficiency clinics and immunological laboratories in these regions.

Computer Database Program

A computerized database program was designed, based on our questionnaire, written with visual Basic language programming and using Access Database software. This software allows data entry of all the information recorded by the referring immunologist on the questionnaire and also allows direct statistical analysis of data.

Patients

The diagnosis of immunodeficiency was based on WHO criteria (2). Only patients with well-established immunodeficiency and the clinical manifestations compatible with their diagnosis were included in our registry. Laboratory analysis for our immunodeficient patients included blood smear, immunoglobulin levels, isohemagglutinins, Schick test, delayed cutaneous hypersensitivity reactions (Manteau test, *Candidia* skin test), lymphocyte subpopulation (T and B) enumeration by flow cytometry method, IgG subclasses titer, chemotaxis evaluation, nitro blue tetrazolium dye test, chemiluminescence, complement component, and hemolytic titration of complement (CH50) as needed.

RESULTS

Four hundred and forty patients with the diagnosis of PID were reported to our center of registry, between March 1999 and March 2001. We had reviewed the patient's records for the last 20 years. All the questionnaires were completed by the immunologists involved in the care of the reported patients. The data were collected from seven different centers, distributed in five large cities of Iran.

Among our patients, predominantly antibody deficiencies were the most common, constituting 45.9% of our patients (n = 202), followed by phagocytic disorders 29.1% (n = 128), T-cell disorders 24.3% (n = 107), and complement deficiencies 0.68% (n = 3) (Fig. 1). Significantly, most of the registered cases were from Children's Medical Center, one of the affiliated hospitals of Tehran University of Medical Sciences (53.2%) (Table I). We found a male to female ratio of 1.7/1. Two thirds of the patients were in pediatric age range (63.4%). The average age of our patients at the time of study was 11.01 years, with the youngest patient referred to our registry 2 months old and the oldest 42 years. The time elapsed between onset of clinical symptoms and PID diagnosis was calculated for some of the PID patients. In general, this interval was considerable, ranging from 41 months for x-linked agammaglobulinemia, 62 months for common variable immunodeficiency, and 79 months for chronic granulomatous disease. Among our 440 patients, 65 patients (14.77%) died. The detailed prevalence of immunodeficiency disorders is presented in Table II.

According to the age of the patients at the time of onset of clinical symptoms, we categorized the main diagnosis of PID by age (Table III). The consanguinity rate among parents of PID patients varied largely. We have calculated this number for PID patients, regsitered

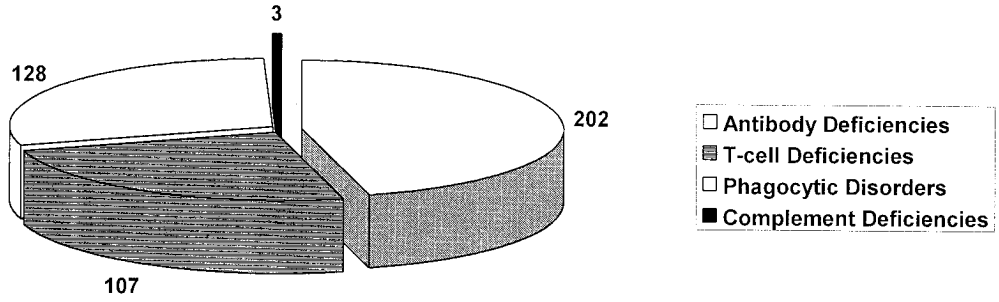

Fig. 1. Registered primary immunodeficient patients (n = 440), according to the system involved, between 1981–2000.

from Children's Medical Center. Overall, consanguinity frequency among parents of PID patients was 64.8%.

Considering the major groups of PID, the rate of relative marriages was higher among our T-cell-deficient patients (77.6%), followed by primary phagocytic disorders (69.3%) and antibody deficiencies (55.9%). Also, the only patient with the diagnosis of complement deficiency had parents who were related. Table IV shows the consanguinity within PID families in detail.

Antibody Deficiencies

The antibody deficiencies were the most frequent immunodeficiency disorder (Table II) reported in 202 cases (45.90%). Common variable immunodeficiency (CVID) was the most frequently reported antibody deficiency (n = 98), including 60 males and 38 females. Pneumonia and upper respiratory tract infections were the most frequent infectious complications in such patients, followed by diarrhea.

X-linked agammaglobulinemia (XLA) was diagnosed in 45 males, which constituted the second-most common humoral immunodeficiency. Their clinical manifestations included upper and lower respiratory tract infections, gastrointestinal infections, meningitis, and arthritis.

Table I. The Number and Percentage of Registered PID Patients from Different Centers of Iran

Name of center	No. of reported pts	Percent
Children's Medical Center (Tehran University)	234	53.18
Daneshvari Hospital (Beheshti University)	19	4.31
Alrasoul Hospital (Iran's University)	37	8.4
Isfahan	55	12.5
Shiraz	71	16.14
Mashhad	13	2.95
Babol	11	2.5
Total	440	100

Forty-two patients with selective IgA deficiency who were clinically symptomatic were registered in IPIDR and ranked third among our humoral immunodeficiencies. The main symptoms observed in these patients were recurrent sinopulmonary infections. There were ten cases of selective IgG subclass deficiency, including six males and four females. All of them had presented with recurrent respiratory infections. There also were five cases of hyper-IgM syndrome and two cases of functional immunoglobulin deficiency.

T-Cell Disorders

T-cell deficiencies were reported in 107 of 440 (24.31%) cases (Table II). Ataxia telangiectasia was the most frequently reported T-cell disorder, constituting 44.85% of cases (n = 48). In this group, there were 21 males and 27 females. Apart from the presence of ataxia and telangiectasia, which were necessary for diagnosis, recurrent respiratory infections constituted the predominant symptoms.

The remainder of T-cell disorders, in the order of frequency, were as follows: combined immunodeficiency (CID) in 15 patients, severe combined immunodeficiency (SCID) in 14 patients, and chronic mucocutaneous candidiasis (CMCC) in 13 patients. We also had 8 cases of Wiskott–Aldrich syndrome, 7 cases of CD4 deficiency, and 2 cases of DiGeorge's syndrome.

Phagocytic Disorders

Phagocytic disorders were the second-most frequent immunodeficiency disorder reported in 128 cases (29.09%) (Table II). Chronic granulomatous disease (CGD) was the most frequent primary defect of phagocytes, with 86 patients (67.18%), including 58 males and 28 females. Consanguinity was found in 29 families with CGD cases. Respiratory infections, including pneumonia, tuberculosis, aspergillosis, and pulmonary abscesses,

Table II. Comparing Data between Iranian Primary Immunodeficiency Registry and Other Registries

	IPIDR[a]	Latin America	Spain
Predominantly Ab deficiency	202 (45.90%)		
X-linked agammaglobulinemia	45 (11.13%)	109 (7.63%)	49 (4.6%)
Common variable ID	98 (22.27%)	154 (10.78%)	213 (19.9%)
Selective IgA deficiency	42 (9.54%)	413 (28.92%)	394 (36.9%)
Selective IgG subclass deficiency	10 (2.27%)	39 (2.73%)	48 (4.5%)
Hyper-IgM syndrome	5 (1.14%)	34 (2.38%)	23 (2.1%)
Functional Ig deficiency	2 (0.45%)	20 (1.4%)	2 (0.2%)
T-cell deficiency	107 (24.31%)		
Severe combined ID	14 (3.18%)	65 (4.55%)	61 (5.7%)
Combined immunodeficiency	15 (3.40%)	4 (0.28%)	
Wiskott–Aldrich syndrome	8 (1.82%)	34 (2.38%)	18 (1.7%)
Ataxia telangiectasia	48 (10.91%)	149 (10.43%)	29 (2.7%)
DiGeorge's syndrome	2 (0.45%)	18 (1.26%)	19 (1.8%)
CD4 deficiency	7 (1.59%)		4 (0.4%)
Chronic mucocutaneous deficiency	13 (2.95%)		19 (1.8%)
Phagosytic disorders	128 (29.09%)		
Leukocyte adhesion defect	13 (2.95%)	3 (0.21%)	4 (0.4%)
Chediac–Higashi syndrome	10 (2.27%)	43 (3.01%)	1 (0.1%)
Chronic granulomatous disease	86 (19.54%)	85 (5.95%)	32 (3%)
Myeloperoxidase deficiency	1 (0.23%)		
Schwachmann's syndrome	4 (0.91%)	1 (0.07%)	
Hyper-IgE syndrome	11 (2.5%)	63 (4.41%)	18 (1.7%)
Kostmann's disease	1 (0.23%)	14 (0.98%)	
Cyclic neutropenia	2 (0.45%)	11 (0.77%)	
Complement deficiency	3 (0.68)	28 (1.96%)	65 (6.1%)
Total	440 (100%)	1428	1069

[a]IPIDR: Iranian Primary Immunodeficiency Registry

made up the most frequent infections in these patients, followed by gasterointestinal tract infections and musculoskeletal infections. Disseminated BCG infection occurred in six cases with CGD.

We also had registered 13 cases of leukocyte adhesion defect (LAD), 11 cases of hyper-IgE syndrome, 4 cases of Swachmann's syndrome, and 2 cases of cyclic neutropenia. We also documented one patient with Kostmann's syndrome and one case with myeloperoxidase deficiency.

Table III. The Main Diagnosis of Primary Immunodeficiencies in Different Age Groups According to the Onset Age of Symptoms

Newborn to early infancy (0–6 months)
Combined immunodeficiency
Severe combined immunodeficiency
Leukocyte adhesion defect
Hyper-IgE syndrome
Schwachmann's syndrome
Early infancy to early childhood (6 months–2 years)
Chediac–Highashi syndrome
Wiskott-Aldrich syndrome
Chronic mucocutaneous candidiasis
X-linked agammaglobulinemia
Selective IgA deficiency
Ataxia telangiectasia
Childhood and adulthood (2 years–adult)
IgG subclass deficiency
Common variable immunodeficiency
Hyper-IgM syndrome
Chronic granulomatous disease

Infections in PID Patients

Survey of registered patients with PIDs in Children's Medical Center showed that infections were the greatest

Table IV. The Frequency of Consanguinity of Primary Immunodeficient Patients, Registered from Children's Medical Center (total number = 234)

Disease	Total number	Relative marriage (%)
Antibody deficiency	118	55.9
X-linked agammaglobulinemia	28	17.8
Common variable immunodeficiency	58	72.1
Selective IgA deficiency	20	52.9
Selective IgG subclass deficiency	8	75
Hyper IgM syndrome	4	50
T-cell defect	60	77.6
Severe combined immunodeficiency	6	83.3
Combined immunodeficiency	5	80
Wiskott-Aldrich syndrome	4	25
Ataxia telangiectasia	39	81.1
Chronic mucocutaneous candidiasis	6	83.3
Phagocytic defect	55	69.3
Leukocyte adhesion defects	10	54.5
Chediac–Higashi syndrome	4	66.7
Chronic granulomatous disease	29	76.3
Schwachmann's syndrome	4	66.7
Hyper-IgE syndrome	8	57.1
Complement deficiency	1	100
Total	234	64.8

Table V. The Frequency of the Most Common Infectious Presentations in Major Divisions of Primary Immunodeficient Patients in Children's Medical Center

No.	Infectious complications	Humoral def. (n = 118)	Cellular def. (n = 60)	Phagocytic def. (n = 55)
1	Pneumonia	87 (73.7%)	41 (68.3%)	32 (58.2%)
2	Otitis media	79 (66.9%)	39 (65%)	20 (36.4%)
3	Sinusitis	90 (80.5%)	45 (75%)	9 (16.4%)
4	Diarrhea	69 (58.8%)	26 (43.3%)	21 (38.2%)
5	Osteomyelitis	4 (3.4%)	2 (3.3%)	7 (12.7%)
6	Septic arthritis	12 (10.2%)	0 (0%)	7 (12.7%)
7	Meningitis/encephalitis	19 (16.1%)	4 (6.7%)	1 (1.9%)
8	Superficial abscess	11 (9.3%)	5 (8.3%)	25 (45.5%)
9	Deep Abscess	8 (6.8%)	0 (0%)	20 (36.4%)
10	Candidiasis	2 (1.7%)	17 (28.3%)	16 (29.1%)
11	BCGosis	0 (0%)	3 (5%)	6 (10.9%)

complication. These infections were seen especially in respiratory tract and gastrointestinal system (Table V). In humoral immunodeficiencies, sinusitis was the most frequent infection (80.5%), pneumonia was the second-most common presentation (73.7%), and otitis media constituted the third (66.9%).

In T-cell deficiencies, sinusitis and pneumonia were the most common infections, being seen in 75% and 68.3%, respectively. Otitis media and recurrent diarrhea with a frequency of 65% and 43.3%, respectively, followed.

In phagocytic disorders, pneumonia was the most frequent (58.2%). Superficial and deep abscesses with a frequency of 45.4% and 36.4% constituted the second and third cause of infections. Also, recurrent diarrhea (38.2%), recurrent otitis media (36.4%), candidiasis (29.1%), and sinusitis (16.4%) were seen.

DISCUSSION

This is the first report of the Iranian Primary Immunodeficiency Registry (IPIDR). We have filled out the questionnaires for 440 patients with the diagnosis of PID during a period of 20 years. This registry, the first of its kind in Iran, is a collaboration of the major universities from all over the country and is supported by Tehran University of Medical Sciences. In fact, construction of such a registry is much more important than for its epidemiological aspect; it can show the health impact of PID and also increase the physician's awareness about such disorders.

All our patients have been diagnosed in the affiliated hospitals of seven universities. The explanation for selecting these universities, as a contributor of this registry, was the existence of clinical immunology clinics and laboratories in these universities. However, it should be noted that the number of patients with PID diagnosis reported in this study does not necessarily reflect the actual prevalence of these diseases, because we have not found all cases of PID disorders and some of the patients with severe forms of disease, such as severe combined immunodeficiency (SCID), die in their early life and they are not marked as immunodeficient patients. More than half the patients are collected from Children's Medical Center, one of the hospitals of Tehran University of Medical Sciences. The Children's Medical Center is a pediatric referral center and most of patients with suspected primary immunodeficiencies are referred to this hospital.

Our registry is hospital-based and we brought the relative frequency of different disorders. We have divided our registered patients in four groups, including antibody deficiencies, T-cell defects, phagocytic disorders and complement deficiencies. Antibody deficiencies were seen in 45% of the registered patients, followed by phagocytic defects seen in 29%. In this study, antibody deficiency was seen in nearly one half of the patients, which is consistent with other studies. Compared with similar studies (8–18), we had a higher frequency of phagocytic system disorders, placing it as the second-most common immunodeficiency, instead of T-cell deficiencies in other studies (8–18).

In Table II, the number and percentage of different primary immunodeficiency disorders diagnosed in Iran and its comparison with other registries is shown (17, 18). This comparison reveals that ataxia telangiectasia (AT) and chronic granulomatous disease (CGD) were much more frequent in our registry than other ones. Also, these disorders can be diagnosed by easy and nonsophisticated tests; however, the higher frequency of these disorders in our registry could be due to the genetic backgrounds in the Iranian population. This idea can be supported by comparing our results with those of our

nearby countries, like Turkey, which has noted a high frequency of ataxia telangiectasia (19).

In contrast to other reports (8–18), we have not found severe combined immunodeficiencies at the same frequency as described. Because of the lack of sufficient knowledge in our general pediatricians, many children with SCID die in their early years of life, before the diagnosis can be made; so we believe that improvement of the pediatricians' knowledge about immunodeficiency disorders is a prerequisite for early diagnosis, and hence mortalities can be prevented more efficiently.

CONCLUSION

The results of our registry reveals that antibody deficiencies is the most frequent diagnosed primary immunodeficiency disorder in Iran. We emphasize that the number of diagnosed patients with PID reported in this study does not reflect the actual prevalence of these disorders, because some of the patients with severe forms of primary immunodeficiencies die in their early life before their diagnosis can be made.

In conclusion, the role of PID registries is important to raise awareness within medical staff to facilitate information concerning new immunodeficiency diseases. To keep the registry active, periodic contact must be maintained with all participants.

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REFERENCES

1. Bruton OC: Agammaglobulinemia. Pediatrics 9:722–728, 1952
2. Rosen FS, Ralph JP, Eibl M, *et al.*: Primary immunodeficiency disease; Report of a WHO scientific group. J Clin Exp Immunol suppl 1:1–28, 1997
3. Conley ME, Stiehm ER: Immunologic disorders in infants and children: General considerations. *In* Immunodeficiency Disorders, ER Stiehm (eds). Philadelphia, WB Saunders, 1996, pp 201–252
4. Stiehm ER, Chin TW, Hass A, *et al.*: Infectious complications of primary immunodeficiencies. Clin Immunol Immunopathol 40:69–86, 1986
5. Webster ABD: Infection in primary immunodeficiency syndrome. Curr Opin Infect Dis 7:444–449, 1994
6. Hermaszewski RA, Webster ABD. Primary hypogammaglobulinaemia: a survey of clinical manifestations and complications. Q J Med 86:31–42, 1993
7. Aghamohammadi A, Strobel S, Novelli V, Holzel H, Morgan J: A single center retrospective 5-year survey of infectious complication in 85 children with combined immunodeficiency. Acta Med Iranica 34 (1,2):7–13, 1996
8. Hayakawa H, Iwata T, Yata J, Kobayashi N: Primary immunodeficiency syndromes in Japan. Overview of a nationwide survey on primary immunodeficiency syndromes. J Clin Immunol 1:31–39, 1981
9. Luzi G, Businco L, Aiuti F: Primary immunodeficiency syndromes in Italy: A report of the national registry in children and adults. J Clin Immunol 3(4):316–320, 1983
10. Hayakawa H, Kobayashi N, Yata J: Primary immunodeficiency diseases and malignancy in Japan. Jpn J Cancer Res 77(1):74–79, 1986
11. Ryser O, Morell A, Hitzig WH.J: Primary immunodeficiencies in Switzerland: First report of the national registry in adults and children. J Clin Immunol 8(6):479–485, 1988
12. Luzi G, Pesce AM, Rinaldi S: Primary immunodeficiencies in Italy. Data revised from the Italian Register of Immunodeficiencies-IRID (1977–88). Allergol Immunopathol (Madr) 19(2):53–57, 1991
13. Gomez L, Yartsev M: Primary immunodeficiencies in the USSR: Update of a nine-year study. Dis Markers 10(1):19–25, 1992
14. Gooi HC: Primary immunodeficiency registry, United Kingdom: Immunodeficiency 4(1–4):191–192, 1993
15. Affentranger P, Morell A, Spath P, Seger R: Registry of primary immunodeficiencies in Switzerland. Immunodeficiency 4(1–4): 193–195, 1993
16. Grumach AS, Duarte AJ, Bellinati-Pires R, *et al.*: Brazilian report on primary immunodeficiencies in children: 166 cases studied over a follow-up time of 15 years. J Clin Immunol 17(4):340–345, 1997
17. Matamoros Flori N, Mila Llambi J, Espanol Boren T, Raga Borja S, Fontan Casariego G: Primary immunodeficiency syndrome in Spain: First report of the National Registry in Children and Adults. J Clin Immunol 17(4):333–339, 1997
18. Zelazko M, Carneiro-Sampaio M, Cornejo de Luigi M, *et al.*: Primary immunodeficiency diseases in Latin America: First report from eight countries participating in the LAGID. Latin American Group for Primary Immunodeficiency Diseases. J Clin Immunol 18(2):161–166, 1998
19. Ersoy F, Berkel AI: Clinical and immunologic studies in 20 families with ataxia telangiectasia. Turk J Pediatr 16:145–160, 1974