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Original Research Article

Clinical and epidemiological characteristics of patients with suspected primary immunodeficiency disorders attending Alexandria University Children's Hospital

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ABSTRACT

Background: Current study was conducted to determine the clinical and epidemiological characteristics of patients with suspected primary immunodeficiencies (PID) seen at Alexandria University Children's Hospital.
Methods: Eighty one patients with suspected PID were seen at Alexandria University Children's Hospital in one year in the period from September 2016 to October 2017. Demographic data of the patients as well as data related to their disease status were taken and evaluation sheet was developed for all patients.
Results: About 61.7% of patients satisfied the criteria of PID based on WHO Scientific Committee. According to modified IUIS classification predominant antibody deficiency was the commonest (34%) followed by other well defined immunodeficiency syndromes (30%), combined immunodeficiencies (16%), phagocytic defects (14%), diseases of immune dysregulation 4% and complement deficiencies (2%). The most frequent disorder was X-linked agammagloulinemia (XLA) (22%). The mean age at diagnosis was 27.4 months. The consanguinity rate was 55.5%. A positive Family history was a strong pointer to diagnosis for PID (46.9%). The commonest clinical presentation was pneumonia (82.7%). 28.4% of patients died from infections. As observed in other patient registries, diagnostic delay remains the major cause of morbidity and mortality.
Conclusions: Primary immunodeficiency disorders are not rare in Egyptian children. Creating awareness of PID should be targeted at hospital pediatricians and families with history of PID and this may reveal more cases within the community. The observed high frequency of combined T- and B-cell immunodeficiencies in this cohort made it a health issue in Egypt as in other developing countries.

Keywords: Clinical presentations, Diagnostic delay, Egypt, Primary immunodeficiency diseases

INTRODUCTION

Primary immunodeficiency diseases (PID) are a diverse group of genetic disorders that affect the immune system. Affected individuals are predisposed to increased rate and severity of infections, allergy, autoimmunity, and malignancy.[1] Early detection of PID is important for timely intervention before serious infections compromise the patient's general condition.[2] However, failure to recognize these conditions remains a major challenge for clinicians worldwide.

The problem is that general practitioners lack familiarity with these rare disorders and lack guidance regarding the appropriate use of immunological investigations.[3] During the last decade, expansive increase in the knowledge of

basic immunology and human genetics has led to recognition of several distinct immunodeficiency disorders and their underlying genetic causes. Currently, there are more than 150 different PIDs recognized by the World Health Organization (WHO).[4]

According to the International Union of Immunological Societies (IUIS) Primary Immunodeficiency Diseases Classification Committee, PID disorders are classified into eight categories:[5]

- Combined T- and B-cell immunodeficiencies
- Predominantly antibody deficiencies
- Other well-defined immunodeficiency syndromes
- Diseases of immune dysregulation
- Congenital defects of phagocyte number, function, or both
- Defects in innate immunity
- Autoinflammatory disorders
- Complement deficiencies.

While most children with recurrent infections have a normal immune system, careful clinical evaluation is crucial for recognition of patients with PIDs.[6] It is important to know the presenting features and warning signs of PID in order to decide the need for further investigations. So, laboratory testing is used to document and delineate the immunologic defect.[7,8]

Epidemiological studies have shown wide geographical variations in terms of prevalence and clinical pattern of immunodeficiency. Many countries worldwide have developed registries to estimate the prevalence and characteristics of different PID phenotypes among their populations.[9-15]

The treatment modalities for PIDs mainly include immunoglobulin replacement, antibiotics and bone marrow transplantation.

Immunoglobulin replacement and judicious use of prophylactic antibiotics can prevent the significant end organ damage and improve long-term outcome and quality of life in many patients with PIDs if diagnosed early.[16,17]

The aim of the present work was to determine the characteristic features and demographic characteristics of various PID disorders among suspected and diagnosed children seen over a one-year period at Alexandria University Children's Hospital.

METHODS

This study conducted on children attending El-Shatby Children's Hospital recruited from Allergy and immunology clinic and the admitted cases of suspected PIDs during the period from September 2016to October 2017 after the approval of the study by ethical committee of Alexandria University.

Inclusion criteria

Patient selection was according to the most current version of the 10 warning signs developed by the Jeffrey Model Foundation.[18] Case diagnosis followed the WHO criteria[4] and according to the International Union of Immunological Societies (IUIS) Primary Immuno-deficiency Diseases Classification Committee.[5]

Exclusion criteria

Patients with secondary causes of immunodeficiency and those with recurrent infections due to other underlying diseases that predispose to frequent infections like AIDS, protein calorie malnutrition, inherited defects like cystic fibrosis, Down syndrome, surgery, environmental conditions like ultraviolet light, chemotherapy, ionizing radiation and chronic hypoxia.[19]

Evaluation sheet was developed for all patients to include data about

- The patients' demographic data, parental consanguinity and family history of PID and/or recurrent infection, previous sib deaths whether unexplained or due to infection
- The child's medical history including history of previous medications, vaccinations, allergies, blood transfusions
- The clinical manifestations suggesting different PIDs, age at onset of symptoms and age at diagnosis of PID if available
- Past history of similar condition (recurrences), other complains including infections, investigations done or treatment received andoutcome each time
- Any abnormal clinical finding elicited during clinical examination was recorded with emphasis on signs known to be associated with certain PID
- Laboratory analyses were performed and included complete blood count with differential cell count, platelet count, examination of peripheral blood smear and C-reactive protein level
- Immunological investigations were done according to each case such as measurement of serum immunoglobulins (IgG, IgA, IgM, and IgE), peripheral blood lymphocyte subsets including the basic panel of T-cell subset (CD3, CD4, CD8), B-cell (CD19) and natural killer cell (CD56/16) by flowcytometry. If required, nitroblue tetrazolium dye testing, oxygen burst test, assessment of the expression of CD18/CD11 on neutrophils by flowcytometry and complement hemolytic activity (CH50) requested.[20,21] Genetic testing was not available in our laboratories and hence was not evaluated.

Statistical analysis

The collected data were coded, tabulated, and statistically analysed using IBM SPSS statistics (statistical package for social sciences) software version 21.0 IBM Corp., Chicago, USA, 2013. Descriptive statistics were done for quantitative data as minimum and maximum of the range as well as mean±SD (standard deviation) for quantitative parametric data, while it was done for qualitative data as number and percentage.

RESULTS

Frequency and distribution of primary immuno-deficiency

In this study, eighty one patients with suspected PID were found over a period of one year but final diagnosis could be reached in about 60% of patients and they were distributed in 13 diseases of five main categories of PID (Figure 1).

No patients were identified in either category of defects in the innate immunity or autoinflammatory disorders. Predominantly antibody deficiencies were the most common (34%). Within this category, X linked agammaglobulinemia, XLA (Brutun's) was the most frequent phenotype (22%). The most common phenotype encountered in the category of other well defined immunodeficiency syndromes was Hyper IgE syndrome (HIGE) (18%).

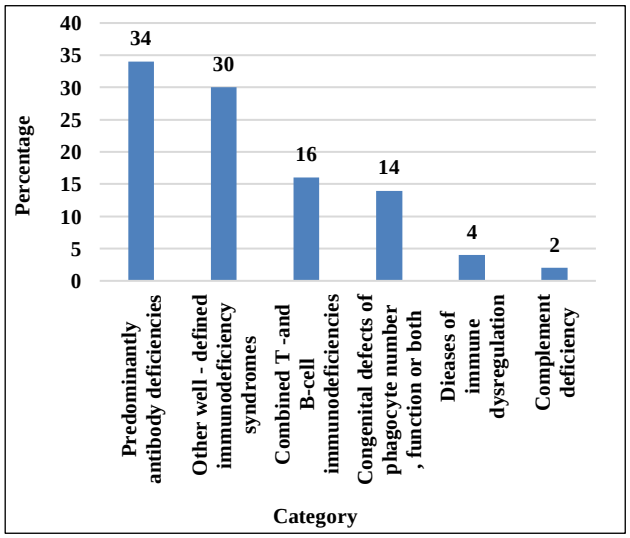

Figure 1: Distribution of diagnosed cases according to classified categories.

Severe combined immunodeficiency (SCID) (12%) was the most common in the combined T and B-cell immunodeficiencies category and chronic granulomatous disease (CGD) (10%) was more common than leukocyte adhesion defect (LAD) in the phagocytic defects category. The frequency and characteristic phenotypes of patients in each PID category are demonstrated in Table 1.

Gender distribution

The study population comprised 58 boys and 23 girls with a male-to-female ratio of 2.5:1. In general we had predominance of male gender in all categories with the highest percentage was found in the predominantly antibody deficiencies (Figure 2). Not only X-linked disorders but also the number of boys has far exceeded that of girls in autosomal disorders as well (Table 2).

Age distribution

In all patients the mean age of onset of symptoms was 9 months (range 0.03-72 months**)**, but it varied between the diagnosed PID categories. (Figure 3).

The mean age at diagnosis for the diagnosed patients (61.7%) was 27 months, and the diagnosis lag, which represents the time elapsed between onset of symptoms and diagnosis, was 16 months.

The minimum age of diagnosis was at the neonatal period (14 days) but the maximum age was 156 months (13 years) with maximum diagnostic delay was 96 months (8 years). No antenatal diagnosis was made. The age at onset of symptoms, age at diagnosis, and the diagnosis lag showed considerable variations between different PID phenotypes (Table 1).

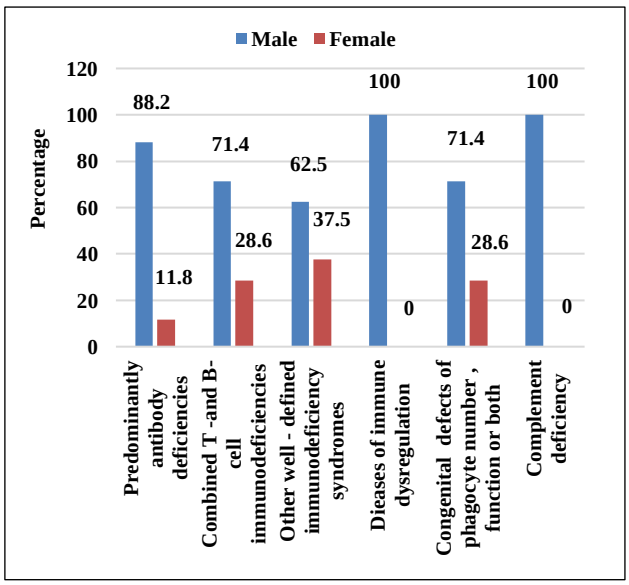

Figure 2: Distribution of diagnosed cases according to gender.

Consanguinity and family history

About 55.5% of patients were products of consanguineous marriages. Family history of death, either unexpected or from infections, or affected family member

by known PID was found in 46.9% of patients with highest percentage in antibody deficiencies (64.7%). Consanguinity and suggestive family history is extremely relevant to PID and varies between different categories and diseases (Table 1).

Table 1: Frequency and characteristics of children with different PID disorders.

Category	Disease	No. of cases (% of total)	Sex boys/girls	Age of Onset (months)[a]	Diagnosis age (months)[a]	Diagnosis lag (months)[a]	Consanguinity (%)	Family history of PID	Mortalities (%)
Predominantly antibody deficiencies		17 (34%)	15/2	18.5 (2-72)	37 (5-156)	18.5 (0.0-84)	8 (47%)	11 (64.7%)	3 (17.6%)
	XLA	11 (22%)	11/0	11 (2-24)	24.5 (5-36)	13.4 (0.0-33)	3 (27%)	9 (81.8%)	3 (27.3%)
	Selective IgA	3 (6%)	2/1	18 (12-24)	32 (24-36)	14 (0.0-24)	2 (66.7%)	0	0
	CVID*	2 (4%)	1/1	66 (60-72)	126 (96-156)	60 (36-84)	2 (100%)	1 (50%)	0
	Hyper IgM syndrome	1 (2%)	1	7	12	5	1	1	0
Combined T-and B-cell immunodeficiencies		8 (16%)	5/3	3.8 (0.47-12)	12 (0.47-48)	8.3 (0.0-36)	6 (75%)	5 (62.5%)	7 (87.5%)
	SCID	6 (12%)	4/2	2.9 (0.47-10)	11 (4-18)	7 (2-16)	4 (66.7%)	4 (66.7%)	6 (100%)
	Omenn syndrome	1 (2%)	1/0	1	2	1	1	1	1
	Mucocutaneous candidiasis	1 (2%)	0/1	12	48	36	1	0	1
Category	**Disease**	**No. of cases (% of total)**	**Sex boys/girls**	**Age of Onset (months)[a]**	**Diagnosis age (months)[a]**	**Diagnosis lag (months)[a]**	**Consanguinity (%)**	**Family history of PID**	**Mortalities (%)**
Other well-defined immunodeficiency syndromes		15 (30%)	10/5	9 (0.03-30)	30 (0.9-126)	21.3 (0.0-96)	9 (60%)	5 (33.3%)	3 (20%)
	Hyper IgE syndrome	9 (18%)	6/3	12.6 (1-30)	47.3 (9-12)	34.6 (2-96)	5 (55.6%)	2 (22%)	1 (11%)
	Digeorge syndrome	5 (10%)	4/1	1.9 (0.03-4)	3.4 (0.9-8)	1.45 (0-8)	3 (60%)	2 (40%)	1 (20%)
	Ataxia telangiectasia	1 (2%)	0/1	12	12	0	1	1	1
Phagocytic defects		7 (14%)	5/2	4.8 (0.6-12)	19.3 (5-54)	14.5 (3-47)	5 (71.4%)	1 (14.3%)	2 (28.6%)
	Chronic granulomatous disease (CGD)	5 (10%)	3/2	6 (1-12)	24.8 (11-54)	18.8 (10-47	4 (80%)	1 (20%)	1 (20%)
	Leukocytic adhesion defects (LAD)	2 (4%)	2/0	1.8 (0.6-3)	5.5 (5-6)	3.7 (3-4.4)	1 (50%)	0	1 (50%)
Diseases of immune dysregulation	Chediak Higashi syndrome	2 (4%)	2/0	9 (6-12)	22.5 (9-36)	13.5 (3-24)	1 (50%)	2 (100%)	1 (50%)
Complement deficiency		1 (2%)	1/0	2	9	7	1	1	0

*: Common variable immunodeficiency, a: Mean (Range).

Table 2: Presenting manifestations of the diagnosed cases.

Diagnosed (n = 50)	Predominantly antibody deficiencies (n = 17)	Combined T-and B-cell immunodeficiencies (n = 8)	Other well-defined immunodeficiency syndromes (n = 15)	Congenital defects of phagocyte number, function or both (n = 7)	Dieases of immune dysregulation (n = 2)	Complement deficiency (n = 1)	^{Mc}p
Failure to thrive	6 (35.3%)	8 (100.0%)	7 (46.6%)	5 (71.4%)	1 (50.0%)	0 (0.0%)	0.032*
Recurrent urti	12 (70.6%)	2 (25%)	8 (53.3%)	1 (14.3%)	1 (50.0%)	0 (0.0%)	0.004*
Otitis media	10 (58.8%)	1 (12.5%)	1 (6.6%)	2 (28.6%)	1 (50.0%)	0 (0.0%)	0.010*
Pneumonia	14 (82.4%)	8 (100.0%)	13 (86.7%)	6 (85.7%)	2 (100.0%)	0 (0.0%)	0.232
Complicated pneumonia	8 (47.1%)	1 (12.5%)	7 (46.6%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0.268
Diarrhea	11 (64.7%)	6 (75%)	6 (40%)	4 (57.1%)	1 (50.0%)	1 (100.0%)	0.259
Meningoencephalitis	4 (23.5%)	4 (50%)	2 (13.3%)	0 (0.0%)	1 (50.0%)	1 (100.0%)	0.031*
Sepsis	5 (29.4%)	8 (100.0%)	9 (60.0%)	5 (71.4%)	1 (50.0%)	1 (100.0%)	0.015*
Supp lymphadenitis	1 (5.9%)	2 (12.5%)	4 (26.7%)	4 (57.1%)	1 (50.0%)	0 (0.0%)	0.008*
Superficial abscess	1 (5.9%)	1 (12.5%)	5 (33.3%)	6 (85.7%)	1 (50.0%)	0 (0.0%)	0.006*
Deep abscess	1 (5.9%)	1 (12.5%)	7 (46.6%)	5 (71.4%)	0 (0.0%)	0 (0.0%)	0.007*
Persistent oral candidiasis	7 (41.2%)	6 (75%)	5 (33.3%)	2 (28.6%)	2 (100.0%)	1 (100.0%)	0.509
Osteomyelitis	0 (0.0%)	1 (12.5%)	1 (6.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.003*
Septic arthritis	2 (11.8)	0 (0.0%)	3 (20%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.009*
Organomegaly	5 (29.4%)	2 (25%)	6 (40%)	6 (85.7%)	2 (100.0%)	0 (0.0%)	0.003*
Lymphadenopathy	4 (23.5%)	0 (00.0%)	6 (40%)	5 (71.4%)	1 (50.0%)	0 (0.0%)	0.301
Lymphoid hypoplasia	12 (70.6%)	7 (87.5%)	3 (20.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.001*
Absent or small thymus	1 (5.9%)	6 (75%)	3 (20.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.001*
Absent tonsils, lnds or adenoids	11 (64.7%)	4 (50%)	1 (6.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.191
Dermatosis and/or dermatitis	9 (52.9%)	5 (62.5%)	8 (53.3%)	5 (71.4%)	2 (100.0%)	1 (100.0%)	0.860
Congenital problems	1 (5.9%)	2 (25%)	11 (73.3%)	0 (0.0%)	1 (50.0%)	0 (0.0%)	<0.001*
Autoimmune	1 (5.9%)	4 (50%)	0 (0.0%)	0 (0.0%)	2 (100.0%)	0 (0.0%)	<0.001*
Allergic	5 (29.4%)	0 (0.0%)	5 (33.3%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0.619

$\chi 2$: Chi square test, MC: Monte Carlo test, *: Statistically significant at $p \leq 0.05$

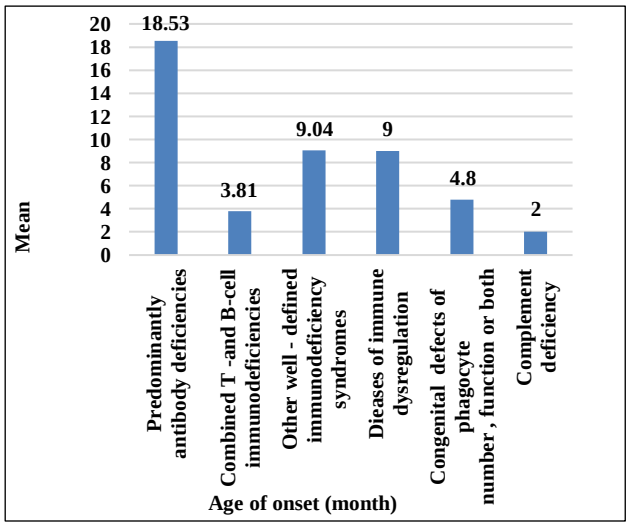

Figure 3: Age of onset of symptoms in diagnosed categories.

Clinical features

PID patients showed a wide spectrum of clinical manifestations (Figure 4). Infection in all sites was the main presentation. Pneumonia was the most common infection in all categories (82.7%) with the highest percentage in the combine group (100%). The presenting manifestations showed considerable variations between different PID categories (Table 2). Regarding individual PID diseases, the present study found that Pneumonia was the most common infection in patients with XLA (90.9%) and all cases had lymphoid hypoplasia (100%). Skin diseases like eczema were frequent in them (63.6%). Mild infections were common in selective IgA deficiency cases like recurrent URTI and diarrhea (100%) and pneumonia found in both CVID cases (100%) from which one case complicated by bronchiectasis. The male child with hyper Ig M syndrome presented with failure to thrive, recurrent otitis media and suppurative lymphadenitis. All cases of SCID presented by failure to

thrive and severe infections like pneumonia, diarrhea and sepsis. Lymphoid hypoplasia was found in 5 cases (83.3%), one case had autoimmune neutropenia and three cases had AIHA from which two cases developed graft versus host disease as a complication of transfusion of non-irradiated packed RBCS. The girl with mucocutaneous candidiasis presented with failure to thrive, pneumonia, sepsis, persistent severe oral candidiasis and disfiguring lesions affecting the skin, nails and scalp with alopecic areas. Candida albicans skin test was negative (diagnostic). A single case of Omenn syndrome presented with failure to thrive, persistent oral candidiasis and exfoliated erythroderma with skin ulcers due to severe staphylococcal skin infection.

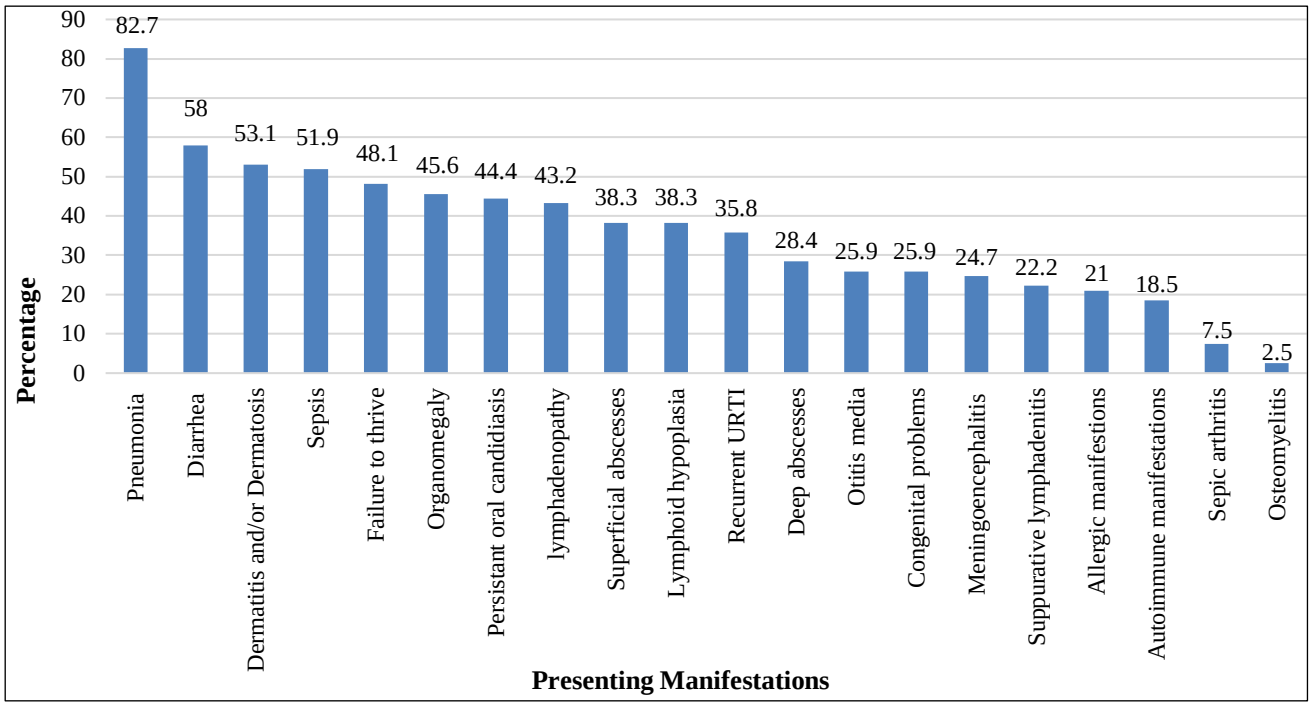

Figure 4: Distribution of the studied cases according to clinical presentation.

In hyper IgE syndrome the most common infection was pneumonia (88.9%). 66.7% of cases presented with deep lung abscesses. Dermatosis and/or dermatitis, skin abscesses, inflammatory eruptions and nonspecific skin rash, were the most common associated clinical findings (77.8%).

In Digeorge syndrome, 80% presented with pneumonia and sepsis. Recurrent URTI, diarrhea and failure to thrive occurred in (60%). All cases (100%) had convulsion and/or tetany due to hypoparathyroidim causing hypocalcaemia, absent thymus was found in 3 cases (60%) when chest X-ray was done. Two cases had dysmorphic features and one had VSD as well. Karyotyping was performed for 3 cases, one had deletion at 22q11.2 chromosome and two cases had few chromosomal breaks. The single case with ataxia-telagiectasia presented with recurrent URTIs, pneumonia, persistent oral candidiasis and failure to thrive. The child had ataxia which deteriorated with age and was associated late with abnormal movement and slurred speech. By examination we found telangiectasia of both eyes.

All cases with CGD presented with deep organ abscesses (100%) with lung abscesses were found in 80% and liver abscesses in 60% of cases. Pneumonia, sepsis, suppurative lymphadenitis and superficial abscesses were the second common (80%), organomegaly was found in 80% of cases and 60% had lymphadenopathy. Screening nitroblue tetrazolium test was positive in two cases and 3 cases had positive oxygen burst test.

The two cases of LAD presented with failure to thrive, pneumonia, diarrhea and recurrent skin abscesses with bad healing (100%). One patient developed severe septicemia and died. History of delayed cord separation for 1 month was found in both cases. Their CBC revealed persistent leukocytosis with absolute neutrophila.

Both cases of Chediak-Higashi presented with pneumonia, persistant oral candidiasis, hepatosplenomegaly and dermatosis in the form of light skin and hair (partial albinism). Their CBC revealed neutropenia with large granules in WBC film, which were the same granules found in BM biopsy.

DISCUSSION

Primary immunodeficiency diseases (PID) represent a class of disorders that affect the development, function, or both of the immune system.[5] Early detection of PID is important for timely intervention before serious infections compromise the patient's general condition.[1, 2]

In the present study, final diagnosis could be reached in about 60% of suspected cases founded over a period of one year while Subbarayan A et al, found that 76% of patients, who presented to two pediatric immunology centers at UK over a period of 10 years, had a defined PID.[22] Under diagnosis occurs because there is no population-based screening process for any PID disorders in Egypt and severe forms of PID such as SCID usually die during infancy before being identified.[3]

The distribution of PIDs in the present study was similar to the ESID registry in the predominance of the category of antibody deficiencies and the frequencies of phagocytic disorders (14%) and diseases of immune dysregulation (4%) while the difference was in the low percentage of antibody deficiencies (34%), in the ESID was 54%.[24-27] This may be because our results represent a single tertiary center study thus the cohort was biased towards the severe forms of PID diseases, consequently, combined T- and B-cell immunodeficiencies constituted 14% of the patients, which is much higher than the ESID registry (8.35%) and registries from European countries and Far-East countries but it was close to the figures reported by some Middle Eastern countries such as Kuwait, Saudi Arabia, Tunisia and Iran.[9-14,23,28,29] This could be due to geographical, ethnic and genetic predisposition of certain PID diseases and the prevalence of consanguineous marriages in this area.[10-12,22-29] Also, this study included a small number of patients who presented at a single tertiary hospital, which made it difficult to evaluate the prevalence of different PID diseases in the entire country.

As regard to individual PID diseases, In this study XLA was the most frequent disorder (22%) which was higher than what was found in Hayakawa H et al study (13.3%) and Lee W study (16.5%) while the selective IgA and CVID were low despite being more common in the ESID[23] and other studies.[9-15,24-28,30] The low percent of CVID founded was probably because our patients were mostly infants and children, while the CVID usually presents at adolescence. In addition, the low percent of selective IgA may be attributed to the fact that those patients usually present by mild symptoms and managed at various outpatient settings. Therefore, it is expected that severe PID phenotypes are more represented in this cohort than mild disorders. As a result, SCID constituted 12% of PIDs in this study showed higher results than Aghamohammadi A et al, study and Noh LM et al, studywho found that the SCID was low (2.4%, 9.6% respectively).[13,31] SCID is especially relevant to Egypt with a lot of patients die in their early life, before the diagnosis can be made.

In the current study, the age of diagnosis for diagnosed patients (60%) ranged from 0.5 to156 months with diagnostic lag up to 96 months. In contrast to Reda SM et al study in which the age of diagnosis ranged from 2 to 108 months with less diagnostic lag up to 72 months.[32] The delay in diagnosis reflects the poor knowledge about PID among general practitioners. In addition, this study found that the median age of onset of symptoms of antibody deficiencies was one year, that of combined B and T-cell defects was 2 months and in phagocytic defects, it was 3 months. The same, Subbarayan A et al, found that B-cell defects presented in late infancy and early childhood while T-cell defects presented at a median age of one month and neutrophil PID also presented early in infancy.[22]

In combined group, the mean age of onset of symptoms of SCID patients was 2.9 months and they were diagnosed at mean age of one year with too long diagnostic lag (7 months), so at the age of diagnosis all of them already catch severe infections and died (100%). The same age of onset was founded by Reda SM et al (2.7 months), but younger age of diagnosis and diagnostic lag (5.7, 3 months respectively).[32] Again, this is due to lack of awareness to early suspect PID. In Egypt, we still have limited experience in stem cell transplantation in immunodeficiency conditions, which may explain the relatively high mortalities among SCID patients.

In relation to gender, the current study found predominance of male gender in all categories. This male predominance was similar to registries of Sweden, Australia, Iran, Kuwait. That is mean that not only in X linked disorders, but also the number of boys has far exceeded that of girls in autosomal disorders as well.[10,13,14,26]

The rate of suggestive family history and the rate of consanguinity founded in the current study was nearly similar to the high rates reported from other Middle Eastern countries.[13,14] An example is the higher prevalence of PID in ethnic Turks living in northwestern Iran.[33] The same, high rates of complement deficiency and CGD have been reported in the Irish Traveller community that, in particular, has high rate of consanguinity and familial cases were found in 25% of combined immunodeficiencies in Swedish children and 31.2% of all PID patients in Australia.[10,26,34]

Regarding the clinical presentations the current study found that pneumonia was the most common infection in all categories with the highest percentage in combined group (100%). Patients with antibody deficiencies presented mainly with pneumonia (82%), recurrent URTI (70%), diarrhea (65%) and otitis media (59%) out of them XLA cases formed about 65% of cases and presented mostly by the same infections. Nearly similar

to Reda SM et al study in which 70% of patients with antibody defects presented by recurrent pneumonia and 33% by recurrent OM and Conley ME et al study in which patients with XLA typically present with recurrent sinopulmonary infections, otitis media and septicemia.[35,36] On the other hand, all patients with combined B-and T- cell defects presented by a combination of pneumonia, failure to thrive and sepsis (100%). Diarrhea and persistent oral candidiasis were common in those patients as well (75%). The same severe presentations were found in SCID patients who constituted 75% of this group. Similar to the study conducted by Madkaikar MM et al who found the same clinical presentations in patients with combined defects.[37]

Pneumonia, superficial and deep abscesses, organomegaly and lymphadenitis were the most common presentations of phagocytic defects from which CGD (71%) was more common than LAD (28%). Similarly Aghamohammadi A et al, found that respiratory infections, including pneumonia, tuberculosis, aspergillosis, and pulmonary abscesses, made up the most frequent infections in these patients, followed by gasterointestinal tract infections, and musculoskeletal infections.[13] Recurrent skin abscesses with bad healing, history of delayed cord separation for 1 month was found in both LAD cases. They presented also by pneumonia, diarrhea and failure to thrive. Repeated blood counts revealed persistent leukocytosis with absolute neutrophila. Similarly, Madkaikar M stated that delayed separation of umbilical cord beyond 2 weeks along with omphalitis and Persistent neutrophilia even in the absence of active infection is suggestive of LAD.[37]

Patients with the hyper IgE syndrome presented by pneumonia (88.9%), deep lung abscesses (66.7%) and dermatosis or dermatitis, either due to infective or allergic process (77.8%). The same, Woellner C stated that eczema, recurrent staphylococcal skin boils and pneumonia with pneumatocele formation are the commonest presenting manifestations of HIES.[38] On the other hand, all cases of Digeorge syndrome had convulsion due to hypocalcemia caused by hypothyroidism. Absent thymus found in 60% of patients, 40% had dysmorphic features and 20% had VSD. Madkaikar M stated that Digeorge syndrome should be suspected in patients with cardiac defects, hypoplastic thymus, hypocalcemia and facial dysmorphism.[37]

CONCLUSION

In conclusion, these data suggest that PID diseases are not rare. The true incidence and prevalence of these conditions will never be known until there is newborn or population screening for these defects. Usually, the only way one knows that an underlying immunodeficiency exists is that the patient develops recurrent or serious infections and is tested for these defects. The current study suggests that these conditions are sufficiently common that primary care physicians are likely to see patients with underlying PID in their practice and should test for these disorders in patients with recurring, unusual or serious infections. In the absence of routine screening, physician awareness of the relative frequency of these disorders is critical to early diagnosis and treatment.

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REFERENCES

1. Conley ME, Notarangelo LD, Etzioni A. Diagnostic criteria for primary immunodeficiencies. Clin Immunol. 1999;93(3):190-7.
2. Champi C. Primary immunodeficiency disorders in children: prompt diagnosis can lead to lifesaving treatment. J Pediatr Heal Care. 2002;16(1):16-21.
3. De Vries E, Clinical Working Party of the European Society for Immunodeficiencies (ESID). Patient-centred screening for primary immunodeficiency: a multi-stage diagnostic protocol designed for non-immunologists. Clin Exp Immunol. 2006;145(2):204-14.
4. Rosen FS, Wedgwood RJP, Eibl M, Fischer A, Aiuti F, Notarangelo L, et al. Primary immunodeficiency diseases: report of a WHO scientific group. Clin Immunol. 1997;109:S1-28.
5. Al-Herz W, Bousfiha A, Casanova JL, Chapel H, Conley ME, Cunningham-Rundles C, et al. Primary immunodeficiency diseases: an update on the classification from the international union of immunological societies expert committee for primary immunodeficiency. Front Immunol. 2011;8(2):54.
6. Lee AY, Gray PE. Evaluating for immunodeficiency in children with recurrent infection. Aus family Physic. 2014;43(9):629-32.
7. O'Sullivan MD, Cant AJ. The 10 warning signs: a time for a change?. Current opin in Allerg Clin Immunol. 2012;12(6):588-94.
8. Comans-Bitter WM, de Groot R, van den Beemd R, Neijens HJ, Hop WC, Groeneveld K, et al. Immunophenotyping of blood lymphocytes in childhood Reference values for lymphocyte subpopulations. J Pediatr. 1997;130(3):388-93.
9. Bejaoui M, Barbouche MR, Sassi A, Larguche B, Miladi N, Bouguerra A, et al. Primary immunodeficiency in Tunisia: study of 152 cases. Arch Pedia organ off Soc francaise Pediatr. 1997;4(9):827-31.
10. Baumgart KW, Britton WJ, Kemp A, French M, Roberton D. The spectrum of primary immunodeficiency disorders in Australia. J Allerg Clin Immunol. 1997;100(3):415-23.
11. Lim DL, Thong BY, Ho SY, Shek LP, Lou J, Leong KP, et al. Primary immunodeficiency diseases in

Singapore-the last 11 years. Singapore Med J. 2003;44(11):579-86.
12. Leiva LE, Zelazco M, Oleastro M, Carneiro-Sampaio M, Condino-Neto A, Costa-Carvalho BT, et al. Primary immunodeficiency diseases in Latin America: the second report of the LAGID registry. J Clin Immunol. 2007;27(1):101-8.
13. Aghamohammadi A, Mohammadinejad P, Abolhassani H, Mirminachi B, Movahedi M, Gharagozlou M, et al. Primary immunodeficiency disorders in Iran: update and new insights from the third report of the national registry. J Clin Immunol. 2014;34(4):478-90.
14. Al-Herz W. Primary immunodeficiency disorders in Kuwait: first report from Kuwait national primary immunodeficiency registry (2004-2006). J Clin Immunol. 2008;28(2):186-9.
15. Boyle JM, Buckley RH. Population prevalence of diagnosed primary immunodeficiency diseases in the United States. J Clin Immunol. 2007;27(5):497-502.
16. Bonagura VR. Using intravenous immunoglobulin (IVIG) to treat patients with primary immune deficiency disease. J Clin Immunol. 2013;33(2):90-4.
17. Slatter MA, Cant AJ. Hematopoietic stem cell transplantation for primary immunodeficiency diseases. Ann NY Acad Sci 2011;1238:122-31.
18. Jeffery Model Foundation 2003. Available at: http://npi. jmfmworld.org. Cited on January 2004.
19. Chinen J, Shearer WT. 6. Secondary immunodeficiencies, including HIV infection. J Allerg Clin Immunol. 2008;121(2):S388-92.
20. Oliveira JB, Fleisher TA. Laboratory evaluation of primary immunodeficiencies. J Allerg Clin Immunol. 2010;125:S297-305.
21. De Vries E, De Bruin-Versteeg S, Comans-Bitter WM, De Groot R, Boerma GJM, Lotgering FK, et al. Longitudinal follow-up of blood lymphocyte 186 sub populations from birth to 1 year of age. J Pedialr 1998;133:586-8.
22. Subbarayan A, Colarusso G, Hughes SM, Gennery AR, Slatter M, Cant AJ, et al. Clinical features that identify children with primary immunodeficiency diseases. Pediatr. 2011;127(5):810-6.
23. Knerr V, Gathmann B, Eades-Perner AM, Kindle G, Grimbacher B. The ESID Online Database for primary immunodeficiencies. First analyses with regard to Germany and Europe. Medizinische Klinik. 2008;103(9):620-7.
24. Mila J, Matamoros N, de Ves Pons J, Raga S, Iglesias JA. The Spanish Registry of primary immunodeficiencies. REDIP-1998. Sangre. 1999;44(2):163-7.
25. Affentranger P, Morell A, Spath P, Seger R. Registry of primary immunodeficiencies in Switzerland. Immunodef. 1993;4(1-4):193.
26. Fasth A. Primary immunodeficiency disorders in Sweden: cases among children, 1974–1979. J Clin Immunol. 1982;2(2):86-92.
27. Luzi G, Businco L, Aiuti F. Primary immunodeficiency syndromes in Italy: a report of the national register in children and adults. J Clin Immunol. 1983;3(4):316-20.
28. Hayakawa H, Iwata T, Yata J, Kobayashi N. Primary immunodeficiency syndrome in Japan. I. Overview of a nationwide survey on primary immunodeficiency syndrome. J Clin Immunol. 1981;1(1):31-9.
29. Al-Attas RA, Rahi AH. Primary antibody deficiency in Arabs: first report from eastern Saudi Arabia. J clin Immunol. 1998;18(5):368-71.
30. Lee WI, Kuo ML, Huang JL, Lin SJ, Wu CJ. Akhil Kakroo. J Clin Immunol. 2005;25(2):162-73.
31. Noh LM, Nasuruddin BA, Abdul Latiff AH, Noah RM, Kamarul Azahar MR, Norzila MZ. Clinical-epidemiological pattern of primary immunodeficiencies in Malaysia 1987–2006: a 20 year experience in Four Malaysian Hospitals. Med J Malaysia. 2013 Feb 1;68(1):13-7.
32. Reda SM, Afifi HM, Amine MM. Primary immunodeficiency diseases in Egyptian children: a single-center study. J Clin Immunol. 2009;29(3):343-51.
33. Shabestari MS, Maljaei SH, Baradaran R, Barzegar M, Hashemi F, Mesri A, et al. Distribution of primary immunodeficiency diseases in the Turk ethnic group, living in the northwestern Iran. J Clin Immunol. 2007;27(5):510-6.
34. Abuzakouk M, Feighery C. Primary immunodeficiency disorders in the Republic of Ireland: first report of the national registry in children and adults. J Clin Immunol. 2005;25(1):73-7.
35. Reda SM, El-Ghoneimy DH, Afifi HM. Clinical predictors of primary immunodeficiency diseases in children. Allerg Asth Immunol Res. 2013;5(2):88-95.
36. Conley ME, Howard V. Clinical findings leading to the diagnosis of X-linked agammaglobulinemia. J Pediatr. 2002;141(4):566-71.
37. Madkaikar M, Currimbhoy Z, Gupta M, Desai M, Rao M. Clinical profile of leukocyte adhesion deficiency type I. Ind Pediatr. 2012;49(1):43-5.
38. Woellner C, Gertz EM, Schäffer AA, Lagos M, Perro M, Glocker EO, et al. Mutations in STAT3 and diagnostic guidelines for hyper-IgE syndrome. J Allerg Clin Immunol. 2010;125(2):424-32.

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