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Primary immunodeficiencies in the Netherlands: National patient data demonstrate the increased risk of malignancy

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Abbreviations: ALPS, Autoimmune lymphoproliferative syndrome; AT, Ataxia telangiectasia; CD, Complement deficiency; CGD, Chronic granulomatous disease; CHH, Cartilage–hair hypoplasia; CHS, Chediak–Higashi syndrome; CMC, Chronic mucocutaneous candidiasis; CN, Cyclic neutropenia; CVID, Common variable immunodeficiency disorder; DGS, DiGeorge syndrome; ESID, European Society for Immunodeficiencies; HIES, Hyper-IgE syndrome; HIGM, Hyper-IgM syndrome; HLH, Hemophagocytic lymphohistiocytosis; HSCT, Hematopoietic stem cell transplantation; LAD, Leukocyte adhesion deficiency; MBL, Mannose-binding lectin; PAD, Predominantly antibody disorder; PID, Primary immunodeficiency; OS, Omenn syndrome; SCID, Severe combined immunodeficiency; SCN, Severe congenital neutropenia; SDS, Shwachman–Diamond syndrome; WAS, Wiskott–Aldrich syndrome; XLA, X-linked agammaglobulinemia; XLP, X-linked lymphoproliferative syndrome; XLT, X-linked thrombocytopenia with mutations in WASP.

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Abstract

Purpose: To analyze the data of the national registry of all Dutch primary immune deficiency (PID) patients, according to the European Society for Immunodeficiencies (ESID) definitions.
Results: In the Netherlands, 745 patients had been registered between 2009 and 2012. An overall prevalence of 4.0 per 100,000 inhabitants was calculated. The most prevalent PID was 'predominantly antibody disorder (PAD)' (60.4%).
In total, 118 transplantations were reported, mostly hematopoietic stem cell transplantations (HSCT). Almost 10% of the PID patients suffered from a malignancy, in particular 'lymphoma' and 'skin cancer'. Compared to the general Dutch population, the relative risk of developing any malignancy was 2.3-fold increased, with a >10-fold increase for some solid tumors (thymus, endocrine organs) and hematological disease (lymphoma, leukemia), varying per disease category.
Conclusions: The incidence rate and characteristics of PID in the Netherlands are similar to those in other European countries. Compared to the general population, PID patients carry an increased risk to develop a malignancy.

1. Introduction

Primary immunodeficiency disorders (PIDs) are rare disorders often associated with genetic defects in the immune system, predisposing individuals to recurrent infections and increased risk of allergy, autoimmunity and malignancy. Over the last decade it has been increasingly recognized that PIDs represent a heterogeneous spectrum of disorders with more than 130 phenotypically distinct PIDs and over 200 disease-related genes identified [1,2].

To increase knowledge on the course and prevalence of PIDs, patient data have been collected over the past years on both the national [3–7] and international levels [8]. These patient cohorts can provide researchers with data on disease manifestations and course, treatment options and efficacy, as well as genetic causes. This information can help to answer relevant questions regarding the prevalence, incidence, disease characteristics and best treatment strategy of the various PIDs [8].

Since 2004, the European Society for Immunodeficiencies (ESID) maintains a pan-European registry for primary immunodeficiencies. To date, more than 16,500 patients have been reported from 30 countries (www.esid.org/registry-number-of-patients). In the Netherlands, data on the national level have been collected from 2009 onwards, using the ESID registry as an online platform in order to gain further knowledge on prevalence, disease characteristics and treatments of PIDs.

Our study presents the outcome of an analysis of all Dutch PID patients entered in the ESID registry as of 2009. The analysis of data on epidemiology, patient characteristics, prevalence of the major PID disease categories, treatment strategies, total number of (stem cell) transplantations, mortality rates and incidence rates of malignancies gives an overview of the Dutch PID population entered in the ESID database between 2009 and 2012. Results are set in perspective with other major cohort studies published earlier.

2. Materials and methods

As an online registry platform, the ESID database was used to collect the national data on PID patients for the Netherlands. The ESID registry has been collecting patient data as a pan-European registry on PIDs since 2004, and has been used by several countries to register their national data on PIDs in the same format. In general, data were entered using a standard web browser with an SSL-protected internet connection and password-protected access, and the patient data were then stored on secure servers. The database system is compliant with data protection and international ethics requirements [9].

Within the ESID registry, PIDs are grouped in nine main categories and subdivided into a total of 70 subcategories. The distribution of PIDs is based on the classification of the International Union of Immunological Societies (IUIS). The main categories used in this article are, in alphabetical order: