Allergol Immunopathol (Madr). 2016;xxx(xx):xxx-xxx

Allergologia et immunopathologia

Sociedad Española de Inmunología Clínica, Alergología y Asma Pediátrica

www.elsevier.es/ai

ORIGINAL ARTICLE

Primary immunodeficiencies in Chile evaluated through ICD-10 coded hospital admissions

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Received 13 January 2016; accepted 27 May 2016

KEYWORDS
Chile;
Hospitalisations;
ICD-10;
Intravenous immunoglobulin;
Primary immunodeficiency

Abstract
Background: The epidemiology and hospitalisation trends of primary immunodeficiency (PID) in Chile are unknown. We aimed to evaluate hospitalisation trends and demographic characteristics of PID admissions in Chile.
Methods: PID admissions between 2001 and 2010 (ICD-10 codes D70.0, D70.4, D71, 72.0, D76.1, D80-D84, E70.3, G11.3) were reviewed using national hospital discharge databases.
Results: During the study period, 5486 admissions due to PID were registered (0.03% of total). 58.5% of patients were male and 66.3% were under 18 years. Median length of stay was one day (range 1-403 days). The most frequent diagnoses were hypogammaglobulinaemia (27.6%), unspecified immunodeficiency (21.9%), haemophagocytic lymphohystiocytosis (18.3%) and common variable immunodeficiency (11.2%). There was a significant increase in PID admission rate and in one-day hospitalisations during this period ($\beta = 0.2$; $P = 0.001$ and $\beta = 33$; $P \leq 0.001$, respectively), however no significant variation was found for longer admissions ($\beta = 4.8$; $P = 0.175$). The increasing trend in PID admission rate was significant in patients with private, but not public insurance ($\beta = 0.53$; $P \leq 0.001$ vs. $\beta = 0.08$; $P = 0.079$, respectively).
Conclusions: We report an increasing trend in admissions due to PID in Chile over a 10-year period. Increase is mainly due to short hospitalisations, possibly accounting for improvements in IVIG access. Higher admission rates in patients with private vs. public insurance suggest socioeconomic disparities in access to PID treatment. ICD-10 coded hospitalisation databases may be useful to determine hospitalisation trends and demographic characteristics of PID admissions worldwide.

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http://dx.doi.org/10.1016/j.aller.2016.05.004
0301-0546/

Introduction

Primary immunodeficiencies (PID) group more than 250 distinct diseases that affect different components and functions of the immune system, predisposing affected individuals to recurrent infections and also to systemic inflammation, hypersensitivity reactions, autoimmunity and cancer.[1,2] The incidence of PID in the general population is approximately 1:2500 live births, and the global prevalence is estimated to vary from 1:1200 to 1:500,000 depending on the population studied.[3–8] The prevalence of PID depends on the type of immune defect, varying from 1:350 for the most prevalent and generally less severe forms, such as antibody deficiencies,[8] to less than 1:1,000,000 for the more rare diseases.[9] Although there has been an increasing trend in improving PID awareness and diagnosis, delayed diagnosis is still frequent[3,7,8,10,11] and many patients probably remain undiagnosed, being subject to infections or complications that impair their quality of life and life expectancy.

Increasing trends in diagnosis of PID worldwide and better access to treatment have improved patients' survival and quality of life. The most prevalent class of PID corresponds to antibody deficiencies, and for this patient group, immunoglobulin replacement is the standard therapy. Immunoglobulin is most frequently administered via the intravenous route (IVIG)[12] even though subcutaneous immunoglobulin administration is also available worldwide.[13] Treatment with IVIG has been shown to increase the life expectancy and reduce both frequency and severity of infections in PID patients,[14–16] improving their quality of life.

In Chile, an increase in physician training and awareness about PID has contributed to improve the diagnosis and management of these patients.[4,10] Despite this improvement, diagnosis is still frequently delayed or incomplete in many cases. Although Chile participates in the Latin American registry of PID, the contributions to this registry are incomplete and very few centres actively register their patients. Therefore, clinical and demographic data on the Chilean population living with PID is missing and studies are needed in order to evaluate the current status of diagnosis and access to treatment.

The Chilean population is a blend of European, mainly Spaniard, and American Indian ethnicities. In economic terms Chile is considered a developing country. Its 2010 gross domestic product per capita was equivalent to about one fourth of that reported in the United States, and it maintains high levels of income inequality. Its current healthcare system was established in the mid-1980s and options for insurance have been described as ''mixed'', consisting of 65–70% public insurance (middle–low socioeconomic level population) and 15–20% private insurance (high socioeconomic level population). During the study period, Chile was divided in thirteen administrative regions from north to south. The Chilean population is unevenly distributed throughout the country, 12% live in the northern regions (I–IV), 62% in the central regions (V–VII and Metropolitan region) and 26% in the southern regions (VIII–XII). The capital city of Santiago, located in the Metropolitan region, concentrates 40% of Chilean population. The majority of immunologists during the period of study worked in academic and private institutions of Santiago, while very few practiced in a few southern regions (VIII and IX) and essentially none were based in the northern regions.

Patients with PID frequently require hospital admissions for diagnostic work-up, management of infectious or other complications, and treatment with IVIG. Furthermore, curative treatment with haematopoietic stem cell transplantation requires costly and prolonged hospital stays and multidisciplinary care at tertiary hospitals. During the study period no home-based therapies for immunoglobulin replacement were practiced yet in Chile, and IVIG would not be covered by insurance if administered as an outpatient therapy. Thus, all patients in Chile requiring IVIG infusions in both, public and private health systems were hospitalised every four weeks in order to receive treatment coverage from the government or health insurance companies. Hospital admission data have been previously reported to be useful to evaluate the epidemiology of PID at a local level.[11,17] However, to the best of our knowledge, there are no population-based epidemiological studies centred on evaluating the characteristics and temporal trends of PID admissions in Latin America. The purpose of this study is to determine hospitalisation trends and demographic characteristics of admissions due to PID in Chile.

Methods

We performed a retrospective review of national hospital discharge databases from the Chilean Ministry of Health to evaluate hospital admissions due to PID during the time period between January 2001 and December 2010.[18] Hospital discharges due to PID were examined using the following ICD-10 codes: D70.0 (congenital agranulocytosis), D70.4 (cyclic neutropenia), D71 (functional disorders of polymorphonuclear neutrophils), D72.0 (genetic anomalies of leukocytes), D76.1 (haemophagocytic lymphohystiocytosis), D80 (hereditary hypogammaglobulinaemia), D81 (combined immunodeficiencies), D82 (Wiskott–Aldrich syndrome), D83 (common variable immunodeficiency), D84 (other immunodeficiencies), E70.3 (Chédiak–Higashi syndrome) and G11.3 (cerebellar ataxia with defective DNA repair). Other admissions coded as neutropenia (ICD-10 code D70; $n = 7404$) were not included in this study due to the inability to differentiate congenital neutropenia from other more common causes unrelated to PID (e.g. neutropenia due to cancer chemotherapy). This database is a mandatory registry of all hospitalisations in the public and private health systems throughout the country. It provides a single main diagnosis per hospitalisation, however, no information on comorbid conditions or treatments administered during the hospital stay are provided. The database has no unique patient identifiers, and thus, does not provide data on incidence or readmissions. Paediatric admissions were defined as those occurring in patients younger than 18 years old, adult admissions were defined as those in patient 18 years old or older.

Statistical analysis

All rates were calculated per 100,000 inhabitants and are shown with 95% confidence intervals (95% CI). Simple linear regressions were used to evaluate the time trends of PID hospitalisations. Unstandardised β coefficients and 95% CI

Please cite this article in press as: Poli C, et al. Primary immunodeficiencies in Chile evaluated through ICD-10 coded hospital admissions. Allergol Immunopathol (Madr). 2016. http://dx.doi.org/10.1016/j.aller.2016.05.004