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ORIGINAL ARTICLE

A 1-Year Prospective French Nationwide Study of Emergency Hospital Admissions in Children and Adults with Primary Immunodeficiency

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Abstract

Purpose Patients with primary immunodeficiency (PID) are at risk of serious complications. However, data on the incidence and causes of emergency hospital admissions are scarce. The primary objective of the present study was to describe emergency hospital admissions among patients with PID, with a view to identifying "at-risk" patient profiles.

Nizar Mahlaoui and Benoit Pilmis contributed equally to this work.

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Methods We performed a prospective observational 12-month multicenter study in France via the CEREDIH network of regional PID reference centers from November 2010 to October 2011. All patients with PIDs requiring emergency hospital admission were included.

Results A total of 200 admissions concerned 137 patients (73 adults and 64 children, 53% of whom had antibody deficiencies). Thirty admissions were reported for 16 hematopoietic stem cell transplantation recipients. When considering the 170 admissions of non-transplant patients, 149 (85%) were related to acute infections (respiratory tract infections and gastrointestinal tract infections in 72 (36%) and 34 (17%) of cases, respectively). Seventy-seven percent of the admissions occurred during winter or spring (December to May). The in-hospital mortality rate was 8.8% (12 patients); death was related to a severe infection in 11 cases (8%) and Epstein-Barr virus–induced lymphoma in 1 case. Patients with a central venous catheter ($n = 19$, 13.9%) were significantly more hospitalized for an infection (94.7%) than for a non-infectious reason (5.3%) ($p = 0.04$).

Conclusion Our data showed that the annual incidence of emergency hospital admission among patients with PID is 3.4%. The leading cause of emergency hospital admission was an acute infection, and having a central venous catheter was associated with a significantly greater risk of admission for an infectious episode.

Keywords Primary immunodeficiency · emergency hospital admission · infection · prophylaxis

Abbreviations

CEREDIH	Centre de Référence des Déficits Immunitaires Héréditaires
CGD	Chronic granulomatous disease
CNS	Central nervous system
COPD	Chronic obstructive pulmonary disease
EBV	Epstein-Barr virus
HRQoL	Health-related quality of life
HSCT	Hematopoietic stem cell transplantation
HSV	Herpes simplex virus
NS	Non-significant
PID	Primary immunodeficiency
RSV	Respiratory syncytial virus

Introduction

Primary immunodeficiency disorder (PID) refers to a heterogeneous group of disorders characterized by an absence or functional impairment in one or more components of the immune system. According to the French national PID registry, the prevalence of patients with PIDs in France is 8 per 100,000 inhabitants. Individuals with PID present with increased susceptibility to infections and an abnormally high frequency of autoimmune, inflammatory, and malignant disorders. However, data on the frequency and causes of emergency hospital admission in this population are scare. This contrasts with other chronic disorders associated with susceptibility to infections, such as chronic obstructive pulmonary disease (COPD) [1], solid organ transplantation [2, 3], hematologic malignancies [4], and HIV infection [5], where the causes of emergency hospital admission, the associated mortality, and the related costs have been studied retrospectively; the resulting information has significantly improved patient care in these fields. We therefore decided to perform a nationwide prospective multicenter study of all consecutive emergency hospital admissions of patients with PID over a 1-year period in France, with a view to identifying risk factors for admission for acute complications.

Methods

Study Design

Between November 1, 2010, and October 31, 2011, we performed a 1-year nationwide prospective observational study (the DIHosp study) in France. The study's primary objective was to record and describe emergency hospital admissions in children (aged 15 or under), adolescents, and adults (aged 16 or over) with PID.

Study Setting

Patients were included through the French national network of PID reference centers (Centre de Référence des Déficits Immunitaires Héréditaires (CEREDIH)). The CEREDIH network was initiated in November 2005 and now comprises 80 medical departments (in 54 different regional centers) with experience in the care of children and/or adults with PID. The CEREDIH registry was launched in November 2005, and data collection is ongoing. Data were initially collected on paper forms and then entered into the European Society for Immunodeficiencies (ESID) online database. The database included demographic information and key medical data, such as the date of PID diagnosis, the date of symptom onset, and a set of clinical laboratory results (see www.ceredih.fr for more details) [6]. Information about the study was e-mailed to each of the 54 centers in July 2010 and also disseminated during a national CEREDIH meeting in September 2010.

Data Collection and Processing Procedures

All emergency hospital admissions reported to CEREDIH centers were included in the study, even when the admission concerned another hospital. In each department, a physician reported the hospital admission on an inclusion form and faxed it to the CEREDIH. On discharge from hospital, the hospital physician filled out a detailed electronic case report form. The following data were collected: major socioeconomic and PID main characteristics, the presence or absence of immunosuppressive therapy or anti-infective prophylaxis, and the patient's medical history (previous infectious events, in particular). We also collected community life data, such as child care arrangements (i.e., whether the patient's child or children stayed at home or, in contrast, mixed with other children at kindergarten or at school), at-risk professions (such as farmers or gardeners), the presence of a pet at home, and any international travel in the previous year.

With regard to the hospital admission, we recorded the severity of the infection, the lab results (notably the white blood cell count and the serum C-reactive protein level), the microbiological data (when available), the outcome, and the final diagnosis. Bloodstream infections were defined according to the Centers for Disease Control and Prevention criteria [7]. In cases with missing data, additional information was systematically collected by the clinical research assistant by careful analysis of the patient's medical records and/or by on-site data collection, if necessary. All statistical analyses were performed using SAS® software (version 9.2, SAS Institute Inc., Cary, NC) and R software (version 3.2.2 [8]). Continuous variables were described as the median (range). Non-parametric tests were used for intergroup comparisons of median values. The threshold for statistical significance was set to $p < 0.05$ in all analyses. Patients newly included in the CEREDIH/ESID database gave their consent to participation; patients who were already registered in the database had given their consent previously. The study's objectives and procedures were approved by the local investigation review board (CPP Ile de France II, Paris, France) on June 7, 2010.

Results

General Description of the Study Population

During the study period, a total of 200 emergency hospital admissions were reported for 137 patients (73 adults; 53.3%). Thirty admissions were reported for 16 (11.7%) patients having undergone hematopoietic stem cell transplantation (HSCT), and so we decided to analyze this specific population separately. A total of 170 emergency hospital admissions were reported for the 121 non-transplant patients. The characteristics of the 16 HSCT recipients and the 17 splenectomized patients are summarized in Supplemental Tables 3 and 4. Sixteen patients (11.6%; 14 children and 2 adults) were diagnosed with a PID during the hospital stay. The admissions peaked during the winter and spring (December to May; Fig. 1).

Data on demographic variables, hospital admissions, and PIDs are summarized in Table 1, and data on environmental risk factors for infections (e.g., international travel and work-related exposure) are presented in Supplemental Table 1.

Comparison of the Hospitalized Group and with the National Registry

We compared the characteristics of the hospitalized patients with those of the patients in the CEREDIH national database in the same year (Supplemental Table 2). The median age was much lower in the hospitalized group than in the CEREDIH group (17.1 [4.1–32.5] vs. 21.6 [6.2–43.1], respectively; $p = 0.04$). The diagnoses in the hospitalized and CEREDIH groups corresponded variously to antibody deficiencies (45% and 53%, respectively; $p = 0.08$), phagocytic disorders (16% in both groups; $p = 1$), and T cell deficiencies (10% and 14%, respectively; $p = 0.25$). Eighty-two patients in the hospitalized group (59.8%) were receiving immunoglobulin (Ig) replacement therapy, with median trough plasma IgG value of 9.6 g/L (range 4.6–67.4), as were 1811 (44.9%) patients in the CEREDIH group ($p < 0.001$), with median trough plasma IgG value of 5.7 g/L (range 0–36.0). As mentioned above, 16 patients (11.7%) in the hospitalized group had undergone HSCT, compared with 431 (10.7%) in the CEREDIH group ($p = 0.67$).

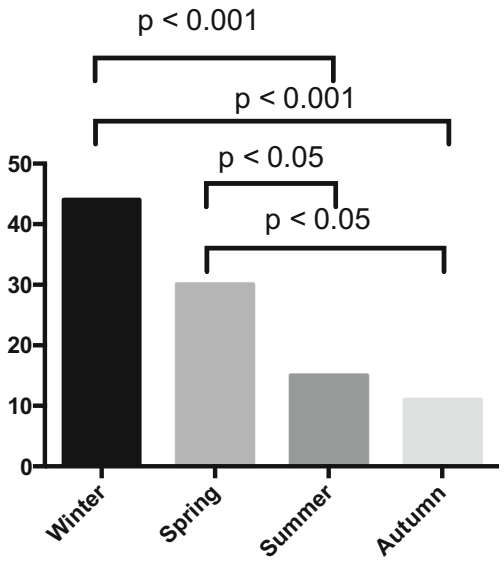

Fig. 1 Seasonal distribution of the 200 emergency hospital admissions of patients with PID (percentages)

Table 1 General characteristics of the 121 non-transplant patients with PID (170 emergency hospital admissions)

	Whole non-transplant population $n = 121$ (%)	Aged 15 or under $n = 46$ (%)	Aged 16 or over $n = 75$ (%)	p value
Age at diagnosis of PID (years) Median (range)	5.1 (0–77.0)	0.8 (0–15.0)	23.5 (0–77.0)	< 0.0001
Number of emergency hospital admissions	170	65	105	< 0.0001
	1 (1–5)	1 (1–4)	1 (1–5)	NS
Number of admissions per patient	7 (1–165)	6 (2–165)	8 (1–79)	NS
Median (range) length of hospital stay				
Type of PID				
Antibody deficiency	55 (45.4%)	9 (19.6%)	46 (61.3%)	<0.0001
Phagocytic disorder	19 (15.7%)	11 (23.9%)	8 (10.7%)	NS
Predominant T cell deficiency	17 (14.0%)	13 (28.3%)	4 (5.3%)	0.0002
PID with immunodysregulation	8 (6.6%)	2 (4.3%)	6 (8.0%)	NS
Other well-defined PIDs	20 (16.5%)	9 (19.6%)	11 (14.7%)	NS
Unclassified PIDs	2 (2%)	2 (4%)	0	NS
Death	11 (9.1%)	5 (10.8%)	6 (8.0%)	NS

Medical History and Administration of Anti-infective Prophylaxis

Seventy-nine of the 121 non-transplant patients (65.3%) had previously presented with a severe infection (affecting the respiratory tract, skin or soft tissue, digestive tract, circulation, or central nervous system (CNS) in, respectively, 56.1%, 17%, 12.2%, 11%, and 3.6% of the cases). The patient's medical history included autoimmunity, bronchiectasis, splenectomy, and hematologic malignancy in, respectively, 36 (29.7%), 31 (25.6%), 16 (13.2%), and 9 (7.4%) cases. Nineteen (13.9%) patients had a central venous catheter. Overall, 97 (71%) patients received antibacterial prophylaxis and 22 patients (16%) received immunosuppressive therapy (Table 2).

Main Symptoms on Admission

Infectious symptoms were reported in 89 of the 121 admissions (73.5%) of non-transplant patients. The infections affected the lungs, gastrointestinal tract, skin/soft tissue, ears/nose/throat, and CNS in, respectively, 37 (30.5%), 18 (14.9%), 17 (14%), 7 (5.8%), and 5 (4.1%) cases. Furthermore, isolated fever was observed for 29 (17%) admissions; all 29 patients had been receiving anti-infective prophylaxis prior to admission. Forty-eight admissions (28.2%) were not ascribed to an infectious event by the attending physician; these were mainly related to hematological disorders and autoimmune or inflammatory events.

Final Diagnoses

Some of the 170 admitted patients were diagnosed with more than one condition, which explains why a total of 175 diagnoses were recorded. A total of 149 infections (64 in children and 85 in adults) were recorded and accounted for 92.7% of the diagnoses in the pediatric population and 80.2% of those in the adult population (p = non-significant (NS)). Twenty-six non-infectious disorders were diagnosed (five in children and 21 in adults): these variously included hematologic disorders (lymphoma, autoimmune hemolytic anemia, idiopathic thrombocytopenic purpura, and autoimmune neutropenia), digestive tract disorders (pancreatitis and cirrhosis with ascites), pulmonary conditions (asthma and pulmonary embolism), neurologic diseases (status epilepticus and severe headache), and other pathologies. Diagnoses and microorganisms found in the hospitalized population are presented by PID and organ system in Tables 3 and 4 and in Fig. 2. The final diagnoses (on discharge) are summarized as a function of the type of PID in Table 3. The microorganisms identified are described according to the type of PID in Table 4, and the distribution of the most frequently observed microorganisms is reported by organ system in Fig. 2.

Treatments and Outcomes in the 121 Non-transplant Patients

Anti-infective agents were administered to 92 (76%) patients, and Ig replacement therapy was initiated in 12 (9.9%) patients (four children and eight adults). Twenty-eight (23.1%) patients were still ill on discharge from hospital, with the persistence (for example) of diarrhea, dyspnea, cutaneous lesions, or

Table 2 Medical history and prophylaxis on admission (n = 121 non-transplant patients)

	Non-transplant patients n = 121 (%)	Aged 15 or under n = 46 (%)	Aged 16 or over n = 75 (%)	p value
Anti-infectious prophylaxis:				
Antibacterial	**86 (71.1)**	**36 (78.3)**	**50 (66.7)**	NS
Cotrimoxazole	50 (41.3)	27 (58.7)	23 (30.7)	
Azithromycin	10 (8.2)	2 (4.3)	8 (10.7)	
Amoxicillin	9 (7.4)	2 (4.3)	7 (9.3)	
Penicillin V	7 (5.8)	3 (6.5)	4 (5.3)	
Other	10 (8.2)	2 (4.3)	8 (10.7)	
Antifungals	**23 (19.0)**	**6 (13.0)**	**17 (22.7)**	NS
Itraconazole	18 (14.9)	4 (8.7)	14 (18.6)	
Other	5 (4.1)	2 (4.3)	3 (4)	
Antivirals	**11 (9.1)**	**1 (2.2)**	**10 (13.3)**	0.051
Valaciclovir	8 (6.6)	0 (0)	8 (10.7)	
Other	3 (2.5)	1 (2.2)	2 (2.7)	
Ig replacement therapy:	**72 (59.5)**	**19 (41.3)**	**53 (70.7)**	*0.002*
Intravenous	46 (38)	14 (30.4)	32 (42.7)	
Subcutaneous	26 (21.5)	5 (10.9)	21 (28)	
Age at initiation				
Median (range)	25.8 (0.1–77.0)	0.9 (0.1–4.8)	38.2 (0.4–77.0)	<0.0001
Trough plasma IgG value (g/L)				
Median (range)	9.6 (4.6–67.4)	8.1 (4.7–67.4)	9.8 (4.6–34)	NS
Immunosuppressive treatment:	**20 (16.5)**	**4 (8.7)**	**16 (21.3)**	NS
Corticosteroids	12 (9.9)	2 (4.3)	10 (13.3)	
Other*	8 (6.6)	2 (4.3)	6 (8)	

In bold the treatment categories received by patients that may be important for infectious events

n = number of answers for this item

*Azathioprine: 3 adults; infliximab: 1 child; rituximab: 1 adult; sirolimus: 1 child

other symptoms. Thirteen (1.1%) patients were transferred to the intensive care unit.

Factors Associated with Emergency Hospital Admission for Infections

During the study period, patients with a central catheter were significantly more likely to be hospitalized for an infection than for a non-infectious condition (94.7% vs. 5.3%, respectively; $p = 0.04$). Patients who had previously experienced a severe infectious episode and patients with bronchiectasis were not significantly more likely to be hospitalized for an infection (p values = 0.08 and 0.23, respectively).

There was no discernible trend linking the use of immunosuppressive drugs to the risk of infections in the hospitalized group. Furthermore, patients hospitalized for infectious complications and those hospitalized for other reasons did not differ significantly with regard to plasma IgG levels on admission.

Deceased Patients

Twelve patients died during their hospital stay (five children and seven adults, including two patients not previously diagnosed with PID). The median age at the time of death was 19.2 years (range 6 months–74 years) overall, 6.5 years for the children, and 31.3 for the adults. With regard to the medical history and comorbidities, 11 patients (91.7%) had previously been hospitalized for a prior severe infection, 5 (42%) had bronchiectasis, 5 (42%) had autoimmune manifestations (including 3 with neutropenia), and 3 (25%) patients had undergone splenectomy. The median length of hospital stay was 41.5 days for patients who died during the hospital stay and 7 days for patients who survived ($p < 0.001$). The deceased patients' characteristics and final diagnoses are summarized in Table 5. It is noteworthy that the causes of death in the two newly diagnosed patients with PID were, respectively, severe respiratory syncytial virus (RSV) infection with *Pseudomonas aeruginosa* pneumonia and severe Epstein-Barr virus (EBV)–related encephalitis.

Table 3 Final diagnoses on discharge following emergency hospital admission, as a function of the type of PID (non-transplant patients)

	Antibody deficiencies $n = 72$ (%)	T cell deficiencies $n = 29$	Phagocytic disorders $n = 29$	Immunodysregulation $n = 7$
Infectious diseases	**62 (84.9)**	**32* (88.9)**	**23 (79.3)**	**5 (71.4)**
Pulmonary	26 (36)	11 (37.9)	6 (20.7)	0 (0)
Digestive	10 (14)	9 (31)	0 (0)	1 (14.3)
Ears/nose/throat	7 (9.7)	1 (3.4)	3 (10.3)	1 (14.3)
Skin and mucosa	1 (1.4)	7 (24)	3 (10.3)	1 (14.3)
Neurologic	3 (4.1)	2 (6.8)	2 (6.9)	1 (14.3)
Bacteremia	4 (5.5)	1 (3.4)	2 (6.9)	0 (0)
Urinary	3 (4.1)	0 (0)	0 (0)	0 (0)
Septic shock	2 (2.8)	0 (0)	0 (0)	0 (0)
Fever	0 (0)	1 (3.4)	2 (6.9)	0 (0)
Miscellaneous*	6 (8.3)	0 (0)	5 (17.2)	1 (14.3)
Non-infectious diseases	**11 (15.1)**	**4 (11.1)**	**6 (20.7)**	**2 (28.6)**
Hematologic	6 (8.3)	0 (0)	1 (3.4)	1 (14.3)
Digestive	0 (0)	2 (6.8)	2 (6.9)	0 (0)
Pulmonary	1 (1.4)	0 (0)	1 (3.4)	1 (14.3)
Neurologic	0 (0)	0 (0)	2 (6.9)	0 (0)
Miscellaneous**	4 (5.5)	2 (6.8)	0 (0)	0 (0)

In bold the categories of final diagnosis

*Miscellaneous final diagnoses (infections): influenza virus, adenitis, EBV infection, and leishmaniasis

**Miscellaneous final diagnoses (other than infectious): anaphylaxis, pulmonary embolism, and granuloma

Discussion

The primary objective of the present study was to describe emergency hospital admissions of patients with PID in France, with a view to identifying "at-risk" patient profiles. The 200 recorded admissions concerned 137 of the 4033 PID patients alive during the study period, giving an incidence of 3.4%. Even though we observed a large number of emergency hospital admissions, this may have been an underestimate; the CEREDIH regional centers might not always have been informed when a patient in the registry was admitted to another establishment. Furthermore, we noted a peak in admissions during the winter and spring. The main reasons for emergency hospital admission were infections (85%)—despite the fact that three-quarters of the patients were already receiving

Table 4 The main pathogens, according to the affected organ (number of documented cases)

Respiratory tract	Digestive tract	Ears/nose/throat	Skin and soft tissue infections	Central nervous system
Streptococcus pneumoniae (7)	*Giardia* (5)	*Pseudomonas aeruginosa* (2)	*Staphylococcus* sp. (5)	*Streptococcus pneumoniae* (2)
Haemophilus influenzae (6)	Rotavirus (3)	*Enterococcus faecalis* (2)	Herpes simplex virus (4)	Enterovirus (1)
Pseudomonas aeruginosa (5)	Cytomegalovirus [3] (2)	*Citrobacter koseri* (1)	*Corynebacteria* (2)	
Staphylococcus spp. (2)	Adenovirus (2)	Rhinovirus (1)	*Streptococcus pyogenes* (2)	
Respiratory syncytial virus (1)	Enterovirus (2)		*Streptococcus anginosus* (1)	
Klebsiella pneumoniae (1)	Epstein-Barr virus (1)		*Actinomyces* spp. (1)	
Moraxella catarrhalis (1)	Norovirus (1)		Anaerobic bacteria (1)	
Nocardia farcinica (1)	*Candida* (1)		Varicella-zoster virus (1)	
	Campylobacter (1)			
	Clostridium difficile (1)			
	Cryptosporidium spp. (1)			

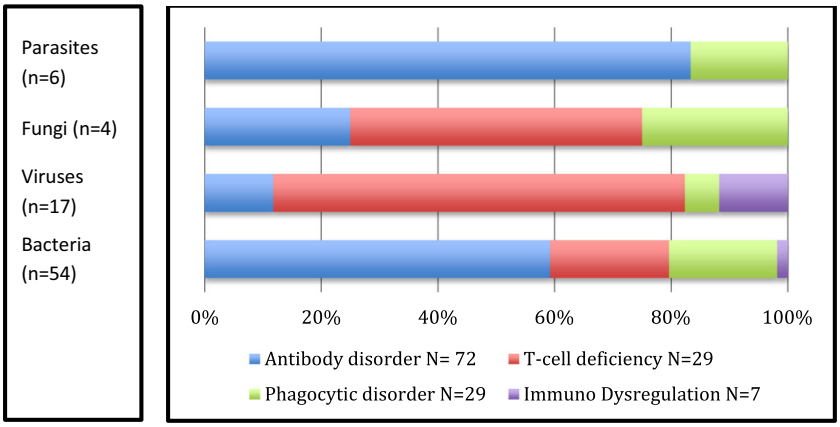

Fig. 2 Microorganisms identified in patients, according to the type of PID (entire study population). The documented parasites were *Giardia* ($n = 5$) and *Cryptosporidium* sp. ($n = 1$). The documented fungal microorganisms were *Aspergillus* ($n = 2$), *Candida* sp. ($n = 1$), and *Pneumocystis* ($n = 1$). The documented viruses were herpes simplex virus ($n = 4$), rotavirus ($n = 3$), enterovirus ($n = 3$), adenovirus ($n = 2$), cytomegalovirus ($n = 2$), Epstein-Barr virus ($n = 1$), norovirus ($n = 1$), rhinovirus ($n = 1$), and varicella-zoster virus ($n = 1$). The documented bacteria were *Streptococcus pneumoniae* ($n = 9$), *Staphylococcus* spp. ($n = 7$), *Pseudomonas aeruginosa* ($n = 7$), *Haemophilus influenzae* ($n = 6$), *Streptococcus* spp. ($n = 3$), *Corynebacteria* ($n = 2$), *Enterococcus faecalis* ($n = 2$), *Campylobacter* spp. ($n = 1$), *Actinomyces* spp. ($n = 1$), *Klebsiella pneumoniae* ($n = 1$), *Moraxella catarrhalis* ($n = 1$), *Nocardia farcinica* ($n = 1$), *Citrobacter koseri* ($n = 1$), *Clostridium difficile* ($n = 1$), anaerobic bacteria (n = 1), and others ($n = 10$)

antibacterial prophylaxis and more than half were already receiving Ig replacement therapy. Most of the infections concerned the lungs and the abdomen. The pathogenic microorganisms (when known) corresponded well to the underlying PID, i.e., bacteria (mainly *Streptococcus pneumoniae)* in patients with antibody deficiencies and viruses or fungi in patients with T cell deficiencies. We could not correctly assess whether these patients were up-to-date for their vaccinations; the latter information was poorly documented by the investigators and was not easily collected by the CEREDIH clinical research assistant. We also noted that a high proportion of respiratory tract infections were due to *Haemophilus influenzae*. Patients with a central venous catheter had a significantly greater risk of emergency hospital admission for infective reason.

In other chronic diseases (such as COPD [9] and heart failure [10]), tools for stratifying the risk of emergency hospital admission or the risk of readmission to hospital in the 12 months following an emergency admission [11] have been developed and validated. Hence, it would be useful to better understand trends in emergency admissions for patients with PID. Many countries have created national PID databases [12–15].The latter generally include data on the prevalence of PIDs, their geographical distribution within the country, age at symptom onset, age at diagnosis, specific genetic diagnoses, distribution of the different types of PIDs, alive or deceased at last follow-up, and the presence or absence of Ig replacement therapy and (occasionally) other long-term therapies. However, these registries are not designed to answer questions about emergency hospital admissions. The results of the DIHosp study broadened our knowledge of the patient's medical history and enabled us to evaluate risk factors for emergency admissions.

Many studies of disease severity fail to measure other patient-centered dimensions, such as social relationships and psychological well-being. It has been reported that poor health-related quality of life (HRQoL) is associated with a twofold increase in the use of acute care resources by patients with chronic conditions [16]. In a recent study of adult patients in the CEREDIH registry, it was found that PIDs had strong negative effects on both physical and mental domains of HRQoL when compared with the French general population [17]. Although HRQoL was not affected by prophylactic treatment (Ig replacement therapy and/or antimicrobial prophylaxis), it was significantly worsened when the patient had been admitted to hospital within the previous 12 months. This finding emphasized the importance of optimizing the clinical management of patients with PID, in order to reduce the risk of hospital admission.

The present study had strengths and limitations. The study's main strength was that it was based on an exhaustively assembled national cohort of patients with PID. The main limitation was intercenter differences in medical practice (particularly with regard to screening for viral pathogens and the anti-infective prophylaxis). Our results prompt us to suggest two new risk factors for emergency hospital admission: the presence of a central venous catheter and seasonality (winter and spring). According the literature data, the risk factors may include a history of severe infections, the number of previous admissions for acute disease, and bronchiectasis. These criteria warrant further investigation.

Table 5 Characteristics of the 12 deceased patients

Deceased patients	Total $n = 12$	Aged 15 or under $n = 5$	Aged 16 or over $n = 7$
Age			
Median (range)	19.2 (0.5–74)	6.5 (0.5–15)	31.3 (17.5–74)
PID			
Common variable immunodeficiency	3	0	3
Combined immunodeficiency	3	2	1
T cell disorder	2	0	2
Hyper-IgE syndrome	1	1	0
Chronic granulomatous disease	1	0	1
Neutropenia	1	1	0
Other	1	1	0
Medical history			
Severe infections	11	4	7
Bronchiectasis	5	0	5
Auto-immunity	5	0	5
Central venous catheter	4	1	3
Splenectomy	3	0	3
Hematologic malignancy	2	1	1
Hematopoietic stem cell transplantation	1	0	1
Other	7	3	4
Treatments			
Immunosuppressive	2	0	2
Antibacterial prophylaxis	8	3	5
Antiviral	4	1	3
Antifungal	2	1	1
Time interval admission/death			
Median (range) (days)	41.5 (1–126)	54 (4–83)	28 (1–126)
Diagnosis			
Septic shock (*Staphylococcus aureus*)	2	0	2
Sepsis	1	1	0
Pneumonia, pericarditis	1	0	1
EBV[1]-induced lymphoma	1	0	1
RSV[2] pneumonia and bacterial superinfection	1	1	0
Bilateral pneumonia	1	0	1
Meningitis	2	1	1
EBV encephalitis	1	1	0
Severe EBV infection	1	1	0
Multiple brain abscesses	1	0	1
Severity criteria at admission			
Respiratory distress	5	1	4
Hemodynamic instability/shock	6	1	5
Neurological distress	2	1	1
Intensive care unit transfer	2	1	1
Cardiac arrest	4	0	4

[1] Epstein-Barr virus

[2] Respiratory syncytial virus

Conclusion

National-level epidemiologic data on patients with PID are scarce. The results of the DIHosp study showed that the incidence of emergency hospital admission among adults and children with PID in France was 3.4%. Most of the infections concerned the lungs and the gastrointestinal tract. The presence of a central venous catheter increased the risk of emergency hospital admission for infective reason. Further studies are required, with a view to determining robust prognostic criteria. Our current findings suggest that HRQoL should be closely monitored in this vulnerable population.

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Compliance with Ethical Standards

Patients newly included in the CEREDIH/ESID database gave their consent to participation; patients who were already registered in the database had given their consent previously. The study's objectives and procedures were approved by the local investigation review board (CPP Ile de France II, Paris, France) on June 7, 2010.

Conflict of Interest The authors declare that they have no conflict of interest.

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