Clinical Infectious Diseases

MAJOR ARTICLE

Prevalence and Etiology of Community-acquired Pneumonia in Immunocompromised Patients

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Background. The correct management of immunocompromised patients with pneumonia is debated. We evaluated the prevalence, risk factors, and characteristics of immunocompromised patients coming from the community with pneumonia.

Methods. We conducted a secondary analysis of an international, multicenter study enrolling adult patients coming from the community with pneumonia and hospitalized in 222 hospitals in 54 countries worldwide. Risk factors for immunocompromise included AIDS, aplastic anemia, asplenia, hematological cancer, chemotherapy, neutropenia, biological drug use, lung transplantation, chronic steroid use, and solid tumor.

Results. At least 1 risk factor for immunocompromise was recorded in 18% of the 3702 patients enrolled. The prevalences of risk factors significantly differed across continents and countries, with chronic steroid use (45%), hematological cancer (25%), and chemotherapy (22%) the most common. Among immunocompromised patients, community-acquired pneumonia (CAP) pathogens were the most frequently identified, and prevalences did not differ from those in immunocompetent patients. Risk factors for immunocompromise were independently associated with neither *Pseudomonas aeruginosa* nor non–community-acquired bacteria. Specific risk factors were independently associated with fungal infections (odds ratio for AIDS and hematological cancer, 15.10 and 4.65, respectively; both $P = .001$), mycobacterial infections (AIDS; $P = .006$), and viral infections other than influenza (hematological cancer, 5.49; $P < .001$).

Conclusions. Our findings could be considered by clinicians in prescribing empiric antibiotic therapy for CAP in immunocompromised patients. Patients with AIDS and hematological cancer admitted with CAP may have higher prevalences of fungi, mycobacteria, and noninfluenza viruses.

Keywords. pneumonia; multidrug-resistant pathogens; microbiology; MRSA; immunocompromise.

During initial evaluation of a patient coming from the community with pneumonia, the identification of possible risk factors for multidrug-resistant organisms or unusual pathogens is crucial [1–3]. Because a microbiological identification is found in about 30% of hospitalized patients with pneumonia coming from the community, and usually requires 24–48 hours to be available, most of patients are treated empirically [4]. Delay in initiation of appropriate empiric antibiotic therapy is a known risk factor for worse clinical outcomes [5–7]; therefore, it is relevant to promptly recognize patients at risk for specific pathogens, specially multidrug-resistant or atypical microbes [1–3].

The aging of the population and advancements in therapeutic protocols have led to an increase prevalence of chronic diseases as well as long-term treatments with immunosuppressive agents [8, 9]. Thus, among patients with pneumonia coming from the community and admitted to the hospital, the number who might not be fully immunocompetent is constantly increasing [8, 9]. Nevertheless, the real prevalence of immunocompromise among patients with pneumonia coming from the community is still unknown. Moreover, guidelines for community-acquired and hospital-acquired pneumonia did not address this topic—what is more, they specifically excluded patients with clinical characteristics determining immunocompromise [5–7], and current evidence in literature is also scarce.

To our knowledge, there are no studies addressing the clinical evaluation and initial empirical antibiotic coverage of patients coming from the community with pneumonia and immunocompromise. Moreover, specific risk factors to assess the causative microbiology and help clinicians choose more appropriate management for these patients have not been clearly identified. Thus, the aim of the current study was to identify the prevalence,

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type, microbiology, and intercorrelations between different risk factors for immunocompromise in hospitalized patients with pneumonia coming from the community.

MATERIALS AND METHODS

Study Design and Population

This is a secondary analysis of the Global Initiative for MRSA Pneumonia (GLIMP) database [10]. The GLIMP study was an international, multicenter, observational, point-prevalence study of adult patients hospitalized for community-onset pneumonia in 54 countries worldwide. Patients were enrolled on a single day during the months of March, April, May, and June 2015. The methods of the GLIMP study have been published elsewhere [10]. The coordinating center (University of Texas Health Science Center, San Antonio) received approval from its institutional review board (No. HSC20150184E).

All adult patients (aged >18 years old) coming from the community and hospitalized with pneumonia during study period were included. Pneumonia was defined as the presence of a new pulmonary infiltrate on chest radiograph at the time of hospitalization, associated with ≥1 of the following criteria: (1) new or increased cough with/without sputum production and/or purulent respiratory secretions, (2) fever or hypothermia, and (3) evidence of systemic inflammation (ie, abnormal white blood cell count or increased C-reactive protein or procalcitonin level). Hospitalized patients with a diagnosis of hospital-acquired or ventilator-associated pneumonia were excluded.

Data Collection

Data were collected from medical records at the time of hospital admission. Data gathered included demographics; respiratory and cardiovascular comorbid conditions; immunocompromised status and other chronic medical conditions; severity of pneumonia (defined as either intensive care unit admission, use of invasive or noninvasive mechanical ventilation, or use of vasopressors/inotropes during the first 24 hours after hospital admission); and specific risk factors for resistant pathogens infection, including chronic aspiration, being bedridden, malnutrition, presence of enteric tube feeding and indwelling catheters (including central venous and urinary catheters), previous infections, chronic microbial colonization, and previous healthcare exposures. The number and type of microbiological samples obtained within 24 hours after hospital admission were also collected. Culture-positive tests, kind of sample, and antibiotic resistance patterns were also gathered, along with empiric antibiotic treatment, given within 24 hours after hospital admission.

Microbiological Workup

Diagnostic testing was performed according to local standard operating procedures and included collection of respiratory and blood cultures and testing for urinary antigens. Microbiological examinations and susceptibility testing were performed according to local standard protocols within the first 24 hours after hospital admission [11]. Multivariable logistic regression models were performed for patients who had a positive culture, to identify specific risk factors for single pathogens.

Causative pathogens were stratified according to the coverage of standard therapy for community-acquired pneumonia (CAP) [5–7]. Those not covered by standard CAP therapy included the following: non–community-acquired bacteria (*Acinetobacter baumanii*, *Enterococcus* vancomycin-resistant, *Nocardia* spp.), mycobacteria, fungi (*Aspergillus fumigatus, Coccidioides, Criptococcus*, *Pneumocystis jirovecii*), and viruses other than influenza [5–7]. Those covered by standard CAP therapy included *Pseudomonas aeruginosa,* methicillin-resistant *Staphylococcus aureus*, methicillin-sensitive *S. aureus*, *Enterobacter* spp., *Enterococcus* spp., *Escherichia coli, Haemophilus influenzae, Klebsiella pneumoniae*, *Moraxella catarrhalis, Proteus mirabilis, Serratia marcescens, Streptococcus pneumoniae, Chlamydia pneumoniae, Mycoplasma pneumoniae, Legionella pneumophilia,* anaerobes bacteria, and influenza viruses. Atypical pathogens included *C. pneumoniae, M. pneumoniae,* and *L. pneumophilia.* CAP therapy was defined as β-lactams (ceftriaxone, ampicillin-sulbactam, amoxicillin-clavulanate, cefepime, ceftazidime, piperacillin-tazobactam) plus macrolide, or fluoroquinolones alone, and, eventually, in association with vancomycin, linezolid, or oseltamivir [5–7].

Definition of Immunocompromised and Study Groups

Immunocompromise was defined as the presence of ≥1 of the following risk factors: (1) AIDS, defined either as human immunodeficiency virus infection with $CD4^+$ lymphocyte count <200/μL or by the occurrence of AIDS-defining conditions; (2) aplastic anemia; (3) asplenia; (4) hematological cancer, defined as lymphoma, acute or chronic leukemia, or multiple myeloma; (5) chemotherapy during the last 3 months; (6) neutropenia, defined as a neutrophil count <500/dL at complete blood cell count; (7) biological drug use (including trastuzumab and therapies for autoimmune diseases, eg, anti–tumor necrosis factor α, prescribed during ≥6 months before hospital admission); (8) lung transplantation; (9) chronic steroid use (>10 mg/d of prednisone or equivalent ≥3 months before hospital admission); (10) lung cancer with either neutropenia or chemotherapy; (11) other solid tumor with either neutropenia or chemotherapy; (12) other immunocompromise (any immunocompromised state, including congenital/genetic immunocompromise and immunosuppressive therapy due to hematological cancer/solid organ transplantation other than lung). Two study groups were identified: those with versus those without 1 risk factor for immunocompromise.

Statistical Analysis

Categorical variables, expressed as counts (percentages), were compared using the χ^2 test. Continuous variables were compared using the unpaired Student *t* test or the Mann-Whitney

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test, when appropriate. Statistical significance was defined as $P < .05$. A network analysis was conducted to represent the frequencies of all immunocompromise variables and their relationships. The size of the circles (the circles visible in Figure 4 [network analysis], each representing a single risk factor for immunocompromise) represents both prevalence of the risk factor and strength of association with other variables.

The predictive value of each variable was categorized by quartiles and analyzed using a univariate regression logistic analysis. A multivariable model was obtained using a Cox regression analysis to identify independent predictors of specific pathogens, using an entry level of P value ≤0.05 and a removal level of P value ≥0.10. Hazard ratios and adjusted analyses were obtained. All statistical analyses were performed with IBM SPSS software (version 22, Statistics for Mac; version 22.0, IBM Crop), and Stata 13 software (StataCorp).

RESULTS

Prevalence of Risk Factors for Immunocompromise

Among 3702 patients enrolled in the GLIMP database, ≥1 risk factor for immunocompromise was identified in 652 (17.6%). The prevalences of patients with pneumonia coming from the community and with ≥1 risk factor for immunocompromise differed among continents and countries, as depicted in Figure 1 and Supplementary Tables 1 and 2. The prevalence of immunocompromise was significantly higher in both North and South America than in the rest of the world (24.0% vs 16.5 [$P < .001$] and 24.8% vs 17.2 [$P = .006$], respectively) (Supplementary Table 1).

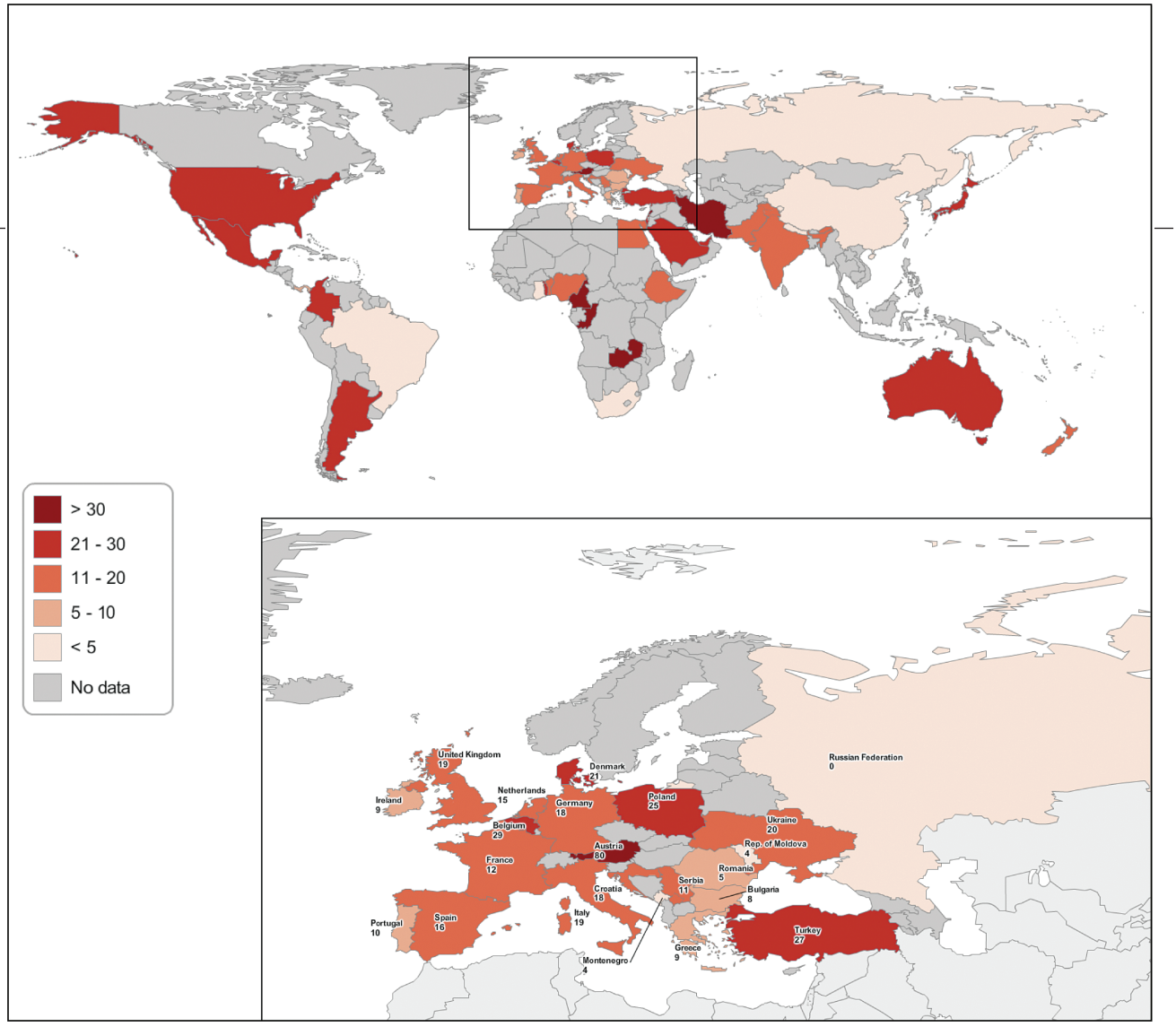

Figure 1. Distribution of prevalence of immunocompromise among the different countries participating in the study, categorized as no data, <5%, 5%–10%, 11%–20%, 21%–30%, or >30% of total cases.

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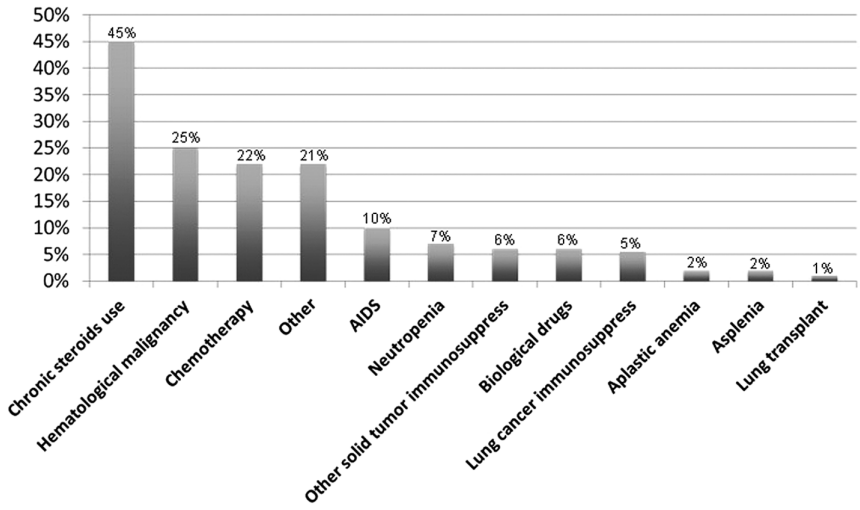

Figure 2. Prevalence of each single risk factor for immunocompromise.

The prevalence of each risk factor for immunocompromise is depicted in Figure 2, with chronic steroid use (45.0%), hematological cancer (25.0%), and chemotherapy (22.0%) being the most frequent ones. A total of 312 patients (8.4%) had >1 risk factor for immunocompromise (Figure 3).

Network Analysis Among Risk Factors for Immunocompromise

The results of the network analysis of all risk factors for immunocompromise are depicted in Figure 4. Relationships were identified between chemotherapy and solid tumor other than lung cancer, hematological cancer, and chronic steroid use, and between other immunocompromise and chronic steroid use.

Clinical and Microbiological Characteristics of Patients With Immunocompromise

Clinical features and disease severity of immunocompetent versus immunocompromised patients are shown in Table 1 and Supplementary Table 3. Immunocompromised patients were significantly younger and malnourished, had a higher frequency of comorbid conditions, previous infections, and colonization by resistant pathogens, and had more frequent contacts with the healthcare system. The prevalences of severe pneumonia did not differ among the 2 study groups.

Microbiological testing was performed in 91.0% (596 of 652) of immunocompromised and 86.0% (2626 of 3050) of immunocompetent patients ($P < .001$). Bacteremia was found in 6.0% (36 of 596) of immunocompromised and 5.5% (145 of 2626; $P = .62$) of immunocompetent patients. At least 1 positive culture was obtained in 40.0% (238 of 596) immunocompromised and 36.0% (935 of 2626) immunocompetent patients ($P = .047$). Microbiological findings are provided in Table 2 and Supplementary Table 4. Among pathogens covered by standard therapy, *P. aeruginosa* was more prevalent in immunocompromised patients (35 [5.9%] vs 98 [3.7%] patients; $P < .02$). Among pathogens not usually covered by standard therapy, immunocompromised patients were more likely to be infected by *Nocardia* spp. (4 [0.7%] vs 0 [0%]

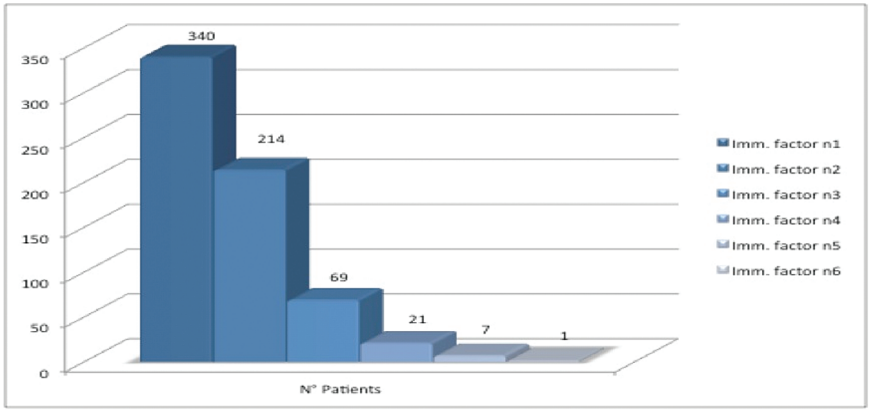

Figure 3. Prevalence of the number of risk factors present simultaneously in a single patient.

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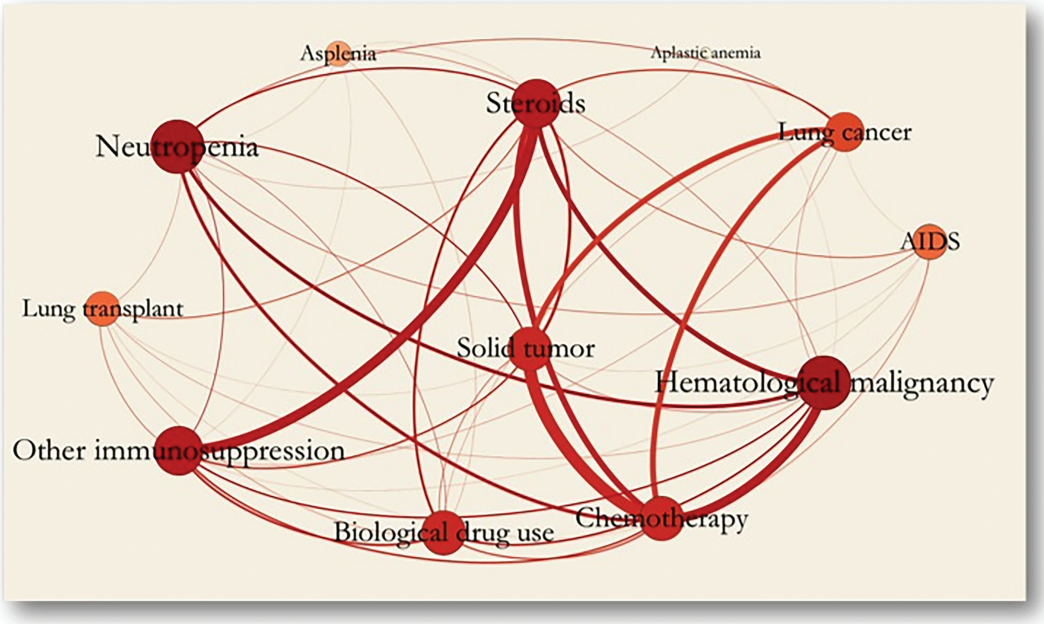

Figure 4. Network analysis between risk factors for immunocompromise.

Table 1. Clinical and Severity Characteristics of the 2 Study Groups (Immunocompetent vs Immunocompromised)

Variable	Patients, No. (%)[a]		*P* Value
	Immunocompetent (n = 3050)	Immunocompromised (n = 652)	
Age, median (IQR)	69 (54–81)	65 (52–74)	<.001
Underweight	125 (6.5)	41 (10.5)	.004
Malnutrition	243 (8.0)	80 (12.3)	<.001
Bedridden	355 (11.6)	60 (9.2)	.04
Chronic aspiration	224 (7.3)	33 (5.1)	.02
Bronchiectasis	136 (4.5)	42 (6.4)	.03
Severe COPD	72 (2.4)	28 (4.3)	.006
Interstitial lung disease	60 (2.0)	35 (5.4)	<.001
Lung transplantation	0 (0.0)	7 (1.1)	<.001
Tracheostomy	37 (1.2)	16 (2.5)	.02
Hypertension	1401 (45.9)	254 (39.0)	.001
Liver disease	103 (3.4)	37 (5.7)	.005
Cirrhosis	50 (1.6)	20 (3.1)	.02
Dementia	372 (12.2)	36 (5.5)	<.001
Enteral tube feeding	36 (1.2)	16 (2.5)	.01
Chronic renal failure	315 (10.3)	85 (13.0)	.04
Hemodialysis	34 (1.1)	18 (2.8)	.001
ICS use	462 (15.2)	128 (19.6)	.005
PPI use	777 (25.5)	251 (38.5)	<.001
Indwelling catheter	52 (1.7)	27 (4.1)	<.001
Prior mycobacteria diseases	70 (2.3)	26 (4.0)	.01
Prior ESBL	39 (1.3)	16 (2.5)	.02
Prior *Pseudomonas*	68 (2.2)	33 (5.1)	<.001
Severe CAP	840 (27.5)	190 (29.1)	.41

Abbreviations: CAP, community-acquired pneumonia; COPD, chronic obstructive pulmonary disease; ESBL, extended-spectrum β-lactamase; ICS, inhaled corticosteroids; IQR, interquartile range; PPI, proton pump inhibitors.

[a]Data represent No. (%) unless otherwise specified.

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Table 2. Pathogens in the 2 Study Groups

Pathogen	Patients, No. (%)		*P* Value
	Immunocompetent (n = 2626)	Immunocompromised (n = 596)	
Pathogens covered by CAP therapy			
Streptococcus pneumoniae	218 (8.3)	50 (8.4)	>.99
Atypical	50 (1.9)	13 (2.2)	.78
Legionella	21 (0.8)	10 (1.7)	.08
MRSA	83 (3.2)	12 (2.0)	.17
MSSA	73 (2.8)	20 (3.4)	.53
Pseudomonas aeruginosa	98 (3.7)	35 (5.9)	.02
Haemophilus influenzae	65 (2.5)	10 (1.7)	.31
Klebsiella pneumoniae	89 (3.4)	22 (3.7)	.81
Influenza virus	126 (4.8)	28 (4.7)	>.99
Pathogens not covered by CAP therapy			
Non-CAP bacteria			
Acinetobacter baumanii	33 (1.3)	7 (1.2)	>.99
Nocardia spp.	0 (0.0)	4 (0.7)	<.001
Mycobacteria			
Mycobacterium tuberculosis	21 (0.8)	5 (0.8)	>.99
NTM	2 (0.1)	5 (0.8)	.002
Fungi			
Aspergillus fumigatus	10 (0.4)	8 (1.3)	.01
Actinomyces	2 (0.1)	0 (0.0)	>.99
Cryptococcus	3 (0.1)	0 (0.0)	.94
Pneumocystis jirovecii	5 (0.2)	13 (2.2)	<.001
Viruses			
Adenovirus	5 (0.2)	0 (0.0)	.62
Coronavirus	3 (0.1)	3 (0.5)	.047
Metapneumovirus	3 (0.1)	2 (0.3)	.51
RSV	7 (0.3)	6 (1.0)	.03
MDR pathogens	231 (8.8)	54 (9.0)	.54

Abbreviations: CAP, community-acquired pneumonia; MDR multidrug-resistant; MRSA methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *S. aureus*; NTM, nontuberculous mycobacteria; RSV, respiratory syncitial virus.

patients; $P < .001$), nontuberculous mycobacteria (NTM) (5 [0.8%] vs 2 [0.1%]; $P < .002$), *A. fumigatus* (8 [1.3%] vs 10 [0.4%]; $P < .01$), *P. jirovecii* (12 [2.0%] vs 5 [0.2%]; $P < .02$), and viruses, such as coronavirus (3 [0.5%] vs 3 [0.1%]; $P < .047$), and respiratory syncytial virus (6 [1.0%] vs 7 [0.3%]; $P < .03$).

Table 3. Multivariable Logistic Regression Analysis

Variable	OR (CI 95%)				
	Pseudomonas aeruginosa	Non-CAP Bacteria	Fungi	*Mycobacterium tuberculosis*	Virus Other Than Influenza
Severe COPD	2.89 (1.34–6.22)	…	…	…	…
Tracheostomy	6.95 (2.87–16.85)	2.91 (1.01–8.38)	…	…	…
ICS use	1.76 (1.09–2.82)	…	…	…	…
Indwelling catheter	2.49 (1.02–6.06)	…	…	…	…
Prior *Pseudomonas*	19.20 (11.71–31.50)	…	…	…	…
COPD	…	1.78 (1.07–2.99)	…	…	…
Severe CAP	…	2.36 (1.42–3.93)	…	…	2.56 (1.27–5.19)
AIDS	…	…	15.10 (6.36–35.88)	…	…
Hematological cancer	…	…	4.65 (1.85–11.69)	…	5.49 (2.20–13.70)
Malnutrition	…	…	…	5.14 (2.21–11.93)	…

Blank cells indicate no statistical significancy.

Abbreviations: CAP community-acquired pneumonia; CI, confidence interval; COPD, chronic obstructive pulmonary disease; ICS, inhaled corticosteroids; OR, odds ratio.

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Once adjusted for confounders, no risk factors of immunocompromise have been recognized for *P. aeruginosa* infection. Likewise, pathogens not covered by usual CAP therapy were found to be associated not with immunocompromise but with chronic obstructive pulmonary disease (odds ratio [OR], 1.78; 95% confidence interval [CI], 1.07–2.99; $P = .03$), tracheostomy (2.91; 1.01–8.38; $P = .048$), and severe pneumonia (2.36; 1.42–3.93; $P = .001$) (Table 3).

Results showed that AIDS (OR, 15.10; 95% CI, 6.36–35.88; $P \leq .001$) and hematological cancer (4.65; 91.85–11.69; $P = .001$) were independently associated with fungal infections; hematological cancer (5.49; 2.20–13.70; $P < .001$) and severe pneumonia (2.56; 1.27–5.19; $P = .009$) with infection by viruses other than influenza; and AIDS (4.41; 1.53–12.73; $P = .006$) and malnutrition (4.50; 2.08–9.72; $P < .001$) with mycobacterial infections. An additional analysis was conducted on mycobacteria, including *M. tuberculosis* and NTM. At multivariable analysis, *M. tuberculosis* was independently associated with malnutrition only (OR, 5.14; 95% CI, 2.21–11.93; $P < .001$). At univariate analysis, patients with AIDS were at higher risk for NTM (23.06; 4.39–121.12; $P < .001$).

A subanalysis was conducted among patients with chronic steroid use versus other risk factors for immunocompromise. Patients with chronic steroid use seemed to be more frequently affected by bacteria not covered by standard CAP therapy (10 [3.4%] vs 1 [0.3%] patients; $P = .002$), *Nocardia* spp. in particular (4 [0.4%] vs 0 [0.0%]; $P = .03$). No differences in the severity of the disease were found (see Supplementary Table 5).

DISCUSSION

The main findings of the present study are as follows: (1) 17.6% of patients admitted with pneumonia from the community have ≥1 risk factor for immunocompromise, with significant differences among continents and countries (ranging from 15.4% to 24.8% by continent and from 80.0% to 4.1% by country); (2) chronic steroid use is by far the most prevalent risk factor leading to immunocompromise, followed by hematological cancer and chemotherapy; (3) 1 of 2 immunocompromised patients has an overlap of ≥2 risk factors, which are also associated between one another in different ways; and (4) the 2 risk factors for immunocompromise independently associated with specific pathogens are AIDS (ie, fungal and mycobacterial infections) and hematological cancer (ie, fungal infection and viral infections other than influenza).

Almost 1 in 5 hospitalized patients with CAP are not immunocompetent. Therefore, it is mandatory to provide clinicians with recommendations or guidelines for the management of hospitalized patients with pneumonia coming from the community who have risk factors for immunocompromise. Currently, there are no guidelines for assessing pneumonia in immunocompromised patients coming from the community. Randomized controlled trials (RCTs) and observational prospective studies are missing owing to the fact that, generally, studies assessing management strategies for pneumonia exclude immunocompromised patients or take into account only a single specific risk factor [12–21]. This lack of information about immunocompromise could lead to both underestimation of the real prevalence with a higher rate of treatment failure and to overestimation and overuse of wide-spectrum antibiotics.

We found a 17.6% global prevalence of immunocompromise among patients coming from the community with pneumonia, with a significantly higher frequency in South and North America. This variability among continents and countries is probably attributable to different healthcare systems and rates of hospitalization of immunocompromised patients. Our analysis showed that the most frequent risk factor for immunocompromise is the chronic use of systemic steroids. Aging of the population and therapeutic advancements have favored the increased burden of chronic diseases and long-term therapies with immunosuppressive agents [8, 9]. In particular, steroids are the agents most frequently prescribed, for their wide spectrum of efficacy in several diseases [13, 17, 19]. Therefore, many patients presenting to the emergency room with pneumonia are receiving chronic steroid treatment. No data are available on this population group, and further studies are needed to characterize these patients and provide individualized management.

Hematological cancer and chemotherapy were other leading immunocompromised factors. These findings are consistent with those in previous studies; patients recruited in observational studies include patients with solid or hematological cancer and those who underwent chemotherapy with associated neutropenia [15–20, 22]. Dedicated guidelines and recommendations are available, especially on respiratory viruses, fungi, and *P. jirovecii* [23–26].

Our network analysis showed that several risk factors for immunocompromise show associations, especially chemotherapy, associated with hematological cancer and solid tumor, and other immunocompromise, associated with chronic steroid use. Moreover, neutropenic patients are well represented and mainly affected also by hematological cancer or under treatment with chemotherapy. Our results suggest that patients may have >1 risk factor characteristic and clinical assessment should be comprehensive, taking into consideration risk factors for immunocompromise and their associated biological mechanisms. In contrast, AIDS, lung transplantation, asplenia, and aplastic anemia seem to be less frequent at admission and to represent distinct clinical entities. Findings of previous studies seem to be in line with our results, with AIDS patients considered as a distinct patient population and with very few observational studies available on asplenia and aplastic anemia [21, 27–31]

In agreement with previous reports, *S. pneumoniae* is the leading microorganism in both immunocompromised and immunocompetent groups [32, 33]. Among pathogens covered by

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standard CAP therapy, only *P. aeruginosa* was more frequently isolated in immunocompromised compared with immunocompetent patients. These findings differ from microbiological results of previous studies. Gram-positive bacteria, especially *S. aureus*, were more frequently identified in patients with immunocompromise of different causes [22, 30, 34]. Only Li and coauthors [13] found patients with immunological disorders, treated with systemic steroids and cytotoxic agents, to have a higher incidence of infections caused by gram-negative bacteria, mainly *P. aeruginosa*. This similarity with our findings could be explained by the prevalence of patients exposed to chronic steroids in our cohort.

Among pathogens not covered by standard CAP therapy, immunocompromised patients were more frequently infected by *Nocardia* spp., NTM, *P. jirovecii*, *A. fumigatus*, and viruses other than influenza. Infections by *P. jirovecii* and NTM are frequently identified in patients with AIDS [35]. *P. jirovecii* is also frequent in other types of immunocompromise, such as solid or hematological cancer in patients who underwent chemotherapy [18, 19, 36]. Fungal infections (eg, *Candida* spp. and *A. fumigatus*) are highly incident in neutropenic hematological cancer patients [22, 37]. Viral infections other than influenza, especially respiratory syncytial virus, are more frequent in patients who underwent hematopoietic stem cell or lung transplantation [38, 39]. Conversely, *Nocardia* spp. infections are mainly described in solid organ transplant recipients [40]. These results, consistent with previous findings, suggest the need for a more in-depth microbiological workup, including community-acquired pathogens and microorganisms not covered by standard therapy.

Surprisingly, we found that risk factors for immunocompromise were not independently associated with *P. aeruginosa* or non–community-acquired bacteria; in contrast, AIDS and hematological cancer are both associated with fungal, mycobacterial, and noninfluenza viral pneumonia, respectively. Empirical therapy should include *P. aeruginosa* coverage, which is highly prevalent in immunocompromised patients. On the contrary, particular attention should be given to fungal, mycobacterial, and viral causes should be for patients admitted with AIDS and hematological cancer [21–29].

Finally, bacteremia rates did not differ between study groups. To our knowledge, there are no studies on bacteremia and immunocompromise in general. The majority of studies have focused on bacteremia in hematopoietic stem cell transplantation, with prevalences varying from 6% to 44% depending on the type of bacteria and host-related factors [41–43]. Few studies addressed this topic in kidney transplant recipients, reporting a prevalence of bacteremia ranging from 25% to 69% [44, 45]. Finally, few studies have addressed HIV and bacteremia, with prevalences ranging from 10% to 25%, depending on the pathogen and grade of immunosuppression [46, 47]. The prevalence of bacteremia in our study was 5T–6% in both immunocompetent and immunocompromised patients. Differences in the prevalence of bacteremia are due mainly to differences between the risk factors for immunocompromise in our study (chronic steroid use, hematological cancer, and chemotherapy) and those previously reported in the literature.

The current study has both limitations and strengths. First of all, to our knowledge, this is the first study showing a worldwide perspective on immunocompromise among patients coming from the community with pneumonia, with a large and diverse sample of patients enrolled across different countries in 6 continents. However, we were not able to involve many investigators from Asia and Africa, and most cases occurred in North America and Europe, thus limiting the generalizability of our findings. Another major limitation is the unfeasibility of grading the severity of immunocompromise and, therefore, stratifying patients and defining the physiopathological interaction between different risk factors, especially with regard to the use of biological drugs and chronic steroids. Furthermore, potentially important risk factors for an immunocompromised state, such as solid organ transplants other than lung, have not been specifically investigated. Finally, no outcome data have been collected, and this strongly limits our speculations as to the correct empiric antibiotic therapy for use in immunocompromised patients with CAP.

In conclusion, our study offers to the scientific community a perspective on immunocompromised patients coming from the community with pneumonia. Future prospective studies on patients with specific risk factors for immunocompromise could provide practical recommendations. In particular, it will be crucial to prepare guidelines on certain prevalent population groups, such as patients exposed to chronic steroids and those with hematological cancer.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Author contributions. M. F. D. P., G. S., S. A., and M. I. R. participated in study design, analysis of data, and writing of the manuscript and take responsibility for the integrity of the work. A. G., D. R., S. T., L. F. R., J. R., J. G. d. C., and F. B. critically reviewed the final manuscript.

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