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Hospital admissions for pyoderma gangrenosum in Spain (1999–2021): Epidemiological and clinical characteristics, temporal trends, and factors associated with poor prognosis and higher cost

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Abstract

Background and Aims: Pyoderma gangrenosum (PG) is a neutrophilic inflammatory dermatosis that can be idiopathic or associated with other diseases. The aim was to analyze the epidemiological and clinical characteristics, temporal trends, risk factors for poor prognosis, and admission costs associated with PG in Spain.

Methods: We conducted a retrospective study, based on the Hospital Discharge Registry of the Spanish National Health System in Spain from 1999 to 2021.

Results: Of 82,161,670 admissions during the study period, 4901 were for PG (hospitalization rate of 59.7/1,000,000 admissions). PG hospitalizations increased from 28.8/1,00,000 in 1999 to 91.9/1,000,000 in 2021. PG was a primary cause of admission in 60.5% of cases, and 58.4% of patients were women. The main PG-related comorbidities were inflammatory bowel disease (15.7%) and neoplasms (10%). There was a significant increase over the years in admissions for inflammatory bowel disease, monoclonal gammopathy of undetermined significance, and lymphoma, as well as an increase in diseases unrelated to PG, such as hypertension, diabetes, and chronic kidney disease. The hospital mortality rate was 5.6%. Death was associated with PG being a primary diagnosis, older age, leukemia, neoplasms, diabetes, and chronic kidney disease. The cost of treatment increased over the years and was higher in older people.

Conclusion: PG cases in the inpatient setting in Spain over the past 23 years make up a tiny proportion of all hospital admissions, although the rate of hospitalization for PG has increased in the last two decades.

KEYWORDS

epidemiology, hospitalization, pyoderma gangrenosum, risk factors, Spain

1 | INTRODUCTION

Pyoderma gangrenosum (PG) is a rare neutrophilic inflammatory dermatosis with an incidence of 3–10 cases per million inhabitants per year; it is more common in adults aged 30–50 years.[1] PG can be idiopathic or associated with other diseases such as inflammatory bowel disease (IBD), rheumatoid arthritis, leukemia, monoclonal gammopathy, or hidradenitis suppurativa; it can also occur as part of syndromes such as PAPA (pyogenic arthritis, PG, and acne).[2]

The pathogenesis of PG is unknown, although it may be related to autoinflammatory deregulation of the innate and adaptive immune systems.[3] PG is often resistant to treatment and has an unpredictable course, as it can evolve independently of or in parallel with the associated disease. Comorbidities unrelated to PG, such as diabetes mellitus, hypertension, and peripheral vascular disease, can negatively affect wound healing and limit treatment options).[4] Most cases require systemic immunosuppressive treatment with corticosteroids, cyclosporine, mycophenolate mofetil, methotrexate, azathioprine, or even biological drugs. The diagnosis of PG is based on clinical presentation and the exclusion of other dermatological diseases.[5] PG has an impact on both morbidity and mortality, and death rates are three times higher among people with uncontrolled PG.[1] These people may need to be hospitalized for therapeutic management with drugs or surgical care of the lesions.[6]

There is a dearth of evidence on the spectrum of PG, as well as the temporal trends and the cost of PG hospital admissions in Spain over the past two decades. The aim of this study was to analyze the epidemiological and clinical characteristics, temporal trends, risk factors for poor prognosis, and admission costs associated with PG in Spain from 1999 to 2021.

2 | METHODS

2.1 | Design and source of data

We conducted a retrospective observational study of people with PG admitted to Spanish hospitals from January 1, 1999 to December 31, 2021, using the Spanish hospital discharge registry (HDR), also known as the minimum basic data set (MBDS) of the Spanish Health Ministry.

The HDR contains information on all people admitted to public hospitals and clinics in the whole of Spain.[7] These data include sex, age, admission and discharge dates, length of hospitalization, Spanish Autonomous Community of the hospital, up to 20 clinical diagnoses for each hospitalization, the circumstances of hospital discharge, and the cost.

The Spanish Health Ministry carries out periodic audits to evaluate the accuracy of the HDR. The (anonymized) data are available on request. Previous studies have used the HDR to evaluate other conditions, including dermatological conditions.[8] It is a valuable resource for estimating current burdens and temporal trends.[9,10]

2.2 | Variables analyzed

We defined the diseases using the International Classification of Diseases (ICD), Ninth Revision, Clinical Modification (ICD-9-CM; 1997–2015); and ICD 10th revision (ICD-10; 2016–2022). ICD-9 and ICD-10 codes are assigned to patients by the clinical documentation unit of each hospital, based on the hospital discharge report. We obtained data for people admitted to hospital with PG by searching for the relevant ICD codes (ICD-9-CM 686.01 and ICD-10 L88).

We analyzed age, sex, length of hospitalization, comorbidities related to PG (IBD, neoplasm, rheumatoid arthritis, leukemia, stoma, monoclonal gammopathy of undetermined significance (MGUS), hidradenitis suppurativa, myelodysplastic syndrome, lymphoma, hepatitis C, Sweet syndrome, Behçet disease, and seronegative spondyloarthropathy), comorbidities unrelated to PG (hypertension, diabetes mellitus, dyslipidemia, chronic kidney disease, obesity, atherosclerosis, and peripheral vascular disease), type of discharge (home/death), diagnosis-related group (DRG), and cost per DRG. DRGs are used to group people with similar clinical conditions and treatment needs. All DRGs fall under two broad categories: surgical or medical (whether the patient underwent a surgical procedure or not). The costs of hospitalization for PG are collected by the Spanish Health Ministry according to the DRG, and are updated every year based on the real costs reported by the Spanish Statistical Office (INE).[11] Supporting Information S1: Table S1 presents the ICD-9-CM and ICD-10 codes for the comorbidities collected.

We defined the hospitalization rate for PG as the number of admissions with PG as a primary diagnosis (listed among the first three diagnoses) or secondary diagnosis (listed in fourth to last position) per 1,000,000 total admissions.

2.3 | Data analysis

We presented categorical variables as absolute values and percentages. For the continuous variables, we calculated means and standard deviations (SDs) if the data were normally distributed according to the Kolmogorov–Smirnov test, or medians and interquartile ranges (IQRs) if they were not.

For the temporal analysis, we grouped the 23 years of the study period into four groups (1999–2004, 2005–2010, 2011–2017, and 2018–2021). To evaluate the linear associations between variables, we used the Chi-square test in 2×4 tables (categorical variables) and the Kruskal–Wallis test (continuous variables). A p-value below 0.05 was considered significant. The measure of association was the odds ratio (OR) with its corresponding 95% confidence interval (CI). We used a multivariable logistic regression analysis to identify independent predictors of mortality. The variables with p-values below 0.05 in the univariate analysis were entered into a multivariable logistic regression using a stepwise selection method with the likelihood ratio test. We used IBM SPSS for Windows v.25.0 (IBM Corp) for all statistical analyses.

2.4 | Ethical aspects

This study did not require the approval of an ethics committee or the informed consent of participants, according to Spanish legislation. To guarantee patient anonymity, the Spanish Health Ministry provided the database after removing all possible patient identifiers.

3 | RESULTS

3.1 | Annual evolution of admissions

During the study period, there were 82,161,670 hospital admissions, of which 4901 were for PG (hospitalization rate 59.7 per 1,000,000). There was a growing trend in PG hospitalizations, from 89 (28.8 per 1,000,000) in 1999 to 320 (91.9 per 1,000,000) in 2021 (Figure 1).

3.2 | Clinical and epidemiological characteristics

From 4901 PG hospitalization, 41.6% were men and 58.4% were women. The median age was 57 years (IQR: 43–72) (Table 1). The main comorbidities related to PG were IBD (15.7%), neoplasm (10.0%), and rheumatoid arthritis (5.2%). Other significant hematological comorbidities included leukemia (3.4%), monoclonal gammopathy of unknown significance (2.7%), myelodysplastic syndrome (1.9%), and lymphoma (1.8%). Other dermatological comorbidities were hidradenitis suppurativa (2.5%) and Sweet syndrome (1.2%) (Table 2). Additionally, 3.4% of patients had a stoma. The main comorbidities unrelated to PG were hypertension (30.8%), diabetes mellitus (19.3%), dyslipidemia (14.5%), chronic kidney disease (8.2%), and obesity (7.8%) (Table 2). PG was the primary diagnosis in 60.5% of admissions. The median length of stay was 12 days. In total, 5.6% of the patients died (Table 1).

3.3 | Differences of primary versus secondary PG diagnosis

From 4901 cases, PG was the primary diagnosis in 60.5% of admissions. Table 3 shows differences in epidemiological characteristics and comorbidities in people admitted to the hospital with PG as a primary or secondary diagnosis. Patients with a primary PG diagnosis were younger (54 vs. 63 years) ($p < 0.001$) and had fewer neoplasms, leukemia, and lymphoma ($p < 0.001$ for each). Additionally, there was a slightly higher prevalence of hidradenitis suppurativa in primary PG diagnoses compared to secondary PG diagnoses ($p = 0.035$). The percentage of other PG-related comorbidities was similar, and those with primary PG diagnoses had lower rates of hypertension, diabetes mellitus, dyslipidemia, chronic kidney disease, obesity, and atherosclerosis ($p < 0.01$ for each).

3.4 | Evolution over the four time periods

Regarding the temporal evolution over the four study periods (Tables 1 and 2), we observed an increase in the median age of people with PG, from 53 years in 1999–2004 to 60 years in 2017–2021 ($p < 0.001$). There was a marked reduction in the youngest age group (20–39 years), from 24% to 8.9% of the total ($p < 0.001$), and an increase in the proportion of people aged 40–59 years (from 28.8% to 36.6%; $p < 0.001$) and those aged 80 years or older (from 7.2% to 16.1%; $p < 0.001$).

We observed a significant increase in admissions for PG with IBD (from 13.2% to 19.3%; $p < 0.001$), stoma (from 1.9% to 4.5%; $p < 0.001$), lymphomas (from 0.5% to 3.6%; $p < 0.001$), and Behçet's disease (from 0% to 1.5%; $p = 0.04$). There was a decrease in admissions for PG with acute leukemia (from 5.6% to 2.8%, $p < 0.001$), and no significant change in admissions for PG with rheumatoid arthritis, seronegative spondyloarthropathy, Sweet syndrome, hidradenitis suppurativa, and hepatitis C.

The data show an increase over the study period in people admitted with PG and hypertension ($p < 0.001$), diabetes mellitus ($p < 0.001$), chronic kidney disease ($p < 0.001$), dyslipidemia ($p < 0.001$), atherosclerosis ($p = 0.002$), and obesity ($p < 0.001$).

The percentage of admissions for a surgical DRG increased between 2005 and 2010 and 2018–2021 (10.6%–17.5%; $p < 0.001$). The median duration of hospitalization decreased over the study period ($p < 0.001$). The percentage of hospital deaths remained stable.

3.5 | Factors associated with mortality

Tables 4 and 5 show the factors associated with mortality in the univariate and multivariable analyses. In the multivariable analysis, the significant factors were having PG as a secondary diagnosis, older age (over 60 years), leukemia, neoplasm, diabetes, and chronic kidney disease. On the other hand, people admitted with IBD had a lower risk of dying.

3.6 | Cost of hospitalization

The median cost of admission for PG was EUR 3781, and this cost increased over the study period. Costs were higher in older people, those who died, those admitted for a surgical DRG, and those who had PG as a secondary diagnosis (Table 6).

4 | DISCUSSION

PG is usually a skin condition managed in the outpatient setting. Some people with severe PG and difficult-to-manage cases require hospital admission, which might be around 10-20%. Our results show the evolution of the most severe PG cases in the inpatient setting in Spain over the past 23 years. We observed an increase

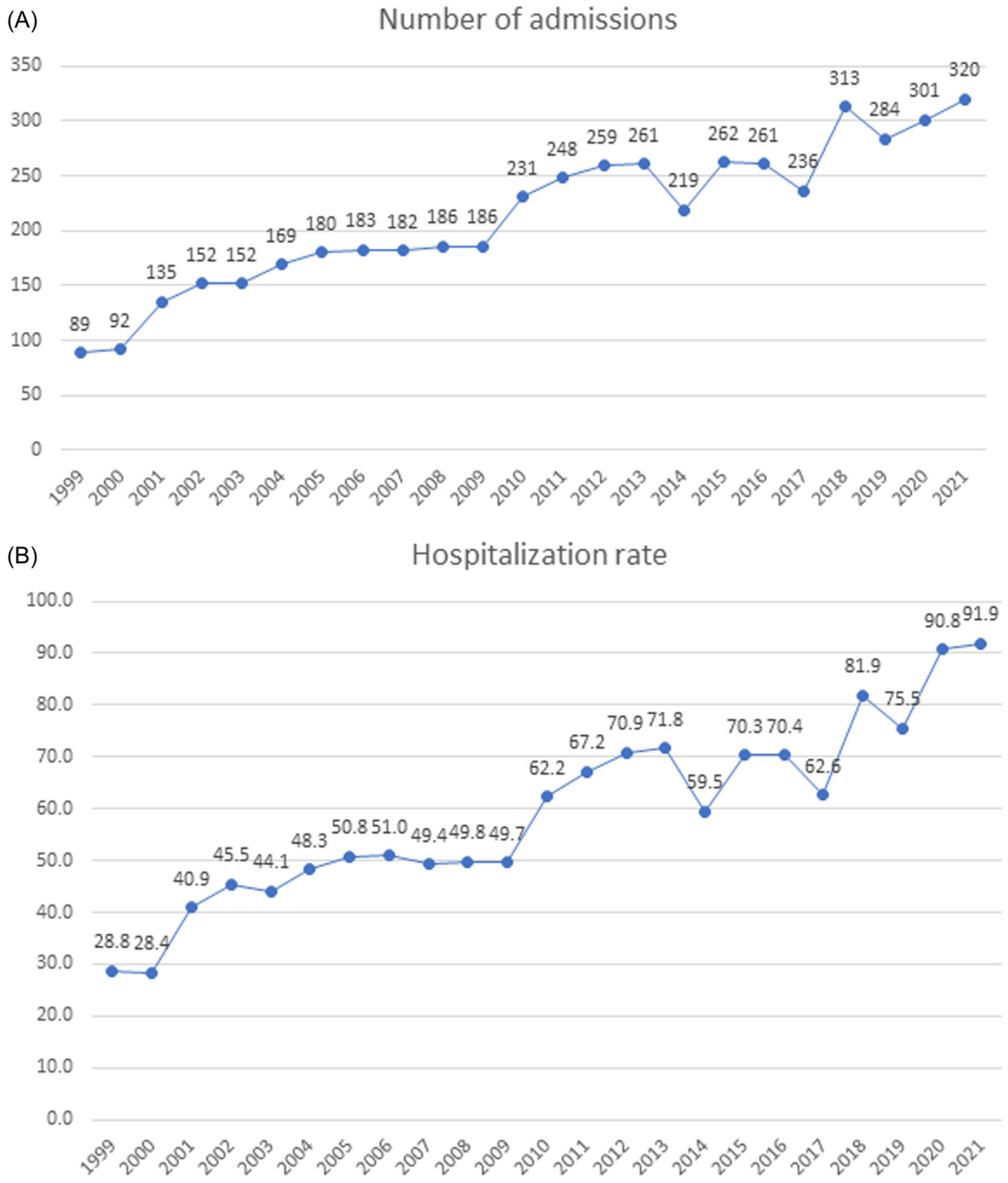

FIGURE 1 (A) Number of admissions for pyoderma gangrenosum in Spain. (B) Rate of admissions for pyoderma gangrenosum (per million total admissions) in Spain.

over the study period in the median age of people admitted with PG, and in the proportion of people admitted with PG who were over 60 years old. Previous studies have observed a similar trend in people admitted for other entities, such as HIV or chronic hepatitis.[9,10] Our results also showed an increase in PG admissions associated with IBD, lymphoma, and MGUS during the study period. The association between PG and IBD is well known, and up to 50% of people with PG will also have IBD.[12] A recent study on the global epidemiology of IBD demonstrated a 49% increase in prevalence from 1999 to 2019,[13] which could explain the increase in associated PG.

We also observed an increase in comorbidities unrelated to PG, particularly cardiovascular risk factors such as hypertension, diabetes, arteriosclerosis, dyslipidemia, and obesity, which may be related to the older age of patients and the increasing burden of these comorbidities in the general population in recent years.[14]

The rate of hospital mortality in our study was 5.6%. PG is associated with increased mortality. A study by Langan and

TABLE 1 Epidemiological characteristics of people admitted to hospital with PG (1999–2021, Spain).

Variable[a]	Total (*n* = 4901)	1999–2004 (*n* = 789)	2005–2010 (*n* = 1148)	2011–2016 (*n* = 1510)	2017–2021 (*n* = 1454)	*p*
Age in years, Mdn (IQR)	57 (43–72)	53 (37–70)	53 (39–71)	57 (44–72)	60 (48–74)	0.001
Age group						
<19 years	174 (3.6)	36 (4.6)	39 (3.4)	50 (3.3)	49 (3.4)	0.721
20–39 years	777 (15.9)	189 (24.0)	251 (21.9)	208 (13.8)	129 (8.9)	0.001
40–59 years	1713 (35.0)	227 (28.8)	393 (34.2)	561 (37.2)	532 (36.6)	0.001
60–79 years	1639 (33.4)	280 (35.5)	348 (30.3)	501 (33.2)	510 (35.1)	0.350
≥80 years	598 (12.2)	57 (7.2)	117 (10.2)	190 (12.6)	234 (16.1)	0.001
Sex						
Men	2039 (41.6)	314 (39.8)	467 (40.7)	629 (41.7)	629 (43.3)	0.523
Women	2862 (58.4)	475 (60.2)	681 (59.3)	881 (58.3)	825 (56.7)	
LOS in days, Mdn (IQR)	12 (6–22)	14(7–26)	12(6–23)	11(6–22)	10 (5–19)	0.001
Type of DRG (*n* = 4107)						
Medical	3525 (85.8)	ND	1026 (89.4)	1300 (86.3)	1.199 (82.5)	0.001
Surgical	582 (14.2)	ND	122 (10.6)	206 (13.7)	254 (17.5)	
Cost in EUR, Mdn (IQR)	3781 (2917–5176)	2797 (2084–3528)	3089 (2600–4771)	4085 (3232–5285)	4288 (3233–6132)	<0.001
PG diagnosis						
Primary[b]	2964 (60.5)	506 (64.1)	704 (61.3)	920 (60.9)	834 (57.4)	0.002
Secondary[c]	1937 (39.5)	283 (35.9)	444 (38.7)	590 (39.1)	620 (42.6)	
Complication and outcome						
Cellulitis	314 (6.4)	30 (3.8)	52 (4.5)	117 (7.7)	115 (7.9)	<0.001
Death	275 (5.6)	41 (5.2)	63 (5.5)	84 (5.6)	87 (6.0)	0.785

Abbreviations: DRG, diagnosis-related group; IQR, interquartile range; LOS, length of hospital stay; Mdn, median; ND, no data; PG, pyoderma gangrenosum.

[a]Presented as *n* (%) unless otherwise specified.

[b]Listed among the first three diagnoses.

[c]Listed in fourth to last position.

TABLE 2 Comorbidities in people admitted to hospital with PG (1999–2021, Spain).

Entity, *n* (%)	Total (*n* = 4901)	1999–2004 (*n* = 789)	2005–2010 (*n* = 1148)	2011–2016 (*n* = 1510)	2017–2021 (*n* = 1454)	*p*
PG-related comorbidities						
IBD	770 (15.7)	104 (13.2)	164 (14.3)	221 (14.6)	281 (19.3)	0.001
Neoplasms	488 (10.0)	73 (9.3)	113 (9.8)	200 (13.2)	102 (7.0)	0.135
Rheumatoid arthritis	254 (5.2)	38 (4.8)	73 (6.4)	86 (5.7)	57 (3.9)	0.112
Leukemia	169 (3.4)	44 (5.6)	45 (3.9)	39 (2.6)	41 (2.8)	0.001
Stoma	165 (3.4)	15 (1.9)	31 (2.7)	53 (3.5)	66 (4.5)	0.001
MGUS	131 (2.7)	7 (0.9)	22 (1.9)	51 (3.4)	51 (3.5)	0.001
Hidradenitis suppurativa	122 (2.5)	13 (1.6)	33 (2.9)	39 (2.6)	37 (2.5)	0.453
Myelodysplastic syndrome	93 (1.9)	0 (0.0)	12 (1.0)	51 (3.4)	30 (2.1)	<0.001
Lymphoma.	86 (1.8)	4 (0.5)	11 (1.0)	18 (1.2)	53 (3.6)	0.001

(Continues)

TABLE 2 (Continued)

Entity, *n* (%)	Total (*n* = 4901)	1999–2004 (*n* = 789)	2005–2010 (*n* = 1148)	2011–2016 (*n* = 1510)	2017–2021 (*n* = 1454)	*p*
Hepatitis C virus	81 (1.7)	19 (2.4)	10 (0.9)	29 (1.9)	23 (1.6)	0.678
Sweet syndrome	61 (1.2)	7 (0.9)	18 (1.6)	21 (1.4)	15 (1.0)	0.452
Behçet's disease	53 (1.1)	0 (0)	17 (1.5)	14 (0.9)	22 (1.5)	0.04
SpA	52 (1.1)	9 (1.1)	18 (1.6)	12 (0.8)	13 (0.9)	0.235
Unrelated comorbidities						
Hypertension	1511 (30.8)	133 (16.9)	258 (22.5)	446 (29.5)	674 (46.4)	<0.001
Diabetes mellitus	946 (19.3)	103 (13.1)	173 (15.1)	309 (20.5)	361 (24.8)	<0.001
Dyslipidemia	711 (14.5)	37 (4.7)	109 (9.5)	226 (15.0)	339 (23.3)	<0.001
Chronis kidney disease	403 (8.2)	27 (3.4)	67 (5.8)	128 (8.5)	181 (12.4)	<0.001
Obesity	383 (7.8)	21 (2.7)	54 (4.7)	136 (9.0)	172 (11.8)	<0.001
Atherosclerosis	163 (3.3)	15 (1.9)	29 (2.5)	52 (3.4)	67 (4.6)	0.002
Peripheral vascular disease	49 (1.0)	2 (0.3)	9 (0.8)	23 (1.5)	15 (1.0)	0.045

Abbreviations: IBD, inflammatory bowel disease; MGUS, monoclonal gammopathy of undetermined significance; PG, pyoderma gangrenosum; SpA, seronegative spondyloarthropathy.

TABLE 3 Epidemiological characteristics and comorbidities of people admitted to hospital with PG as primary or secondary diagnosis (1999–2021, Spain).

Variable	Primary PG diagnosis (*n* = 2964)	Secondary PG diagnosis (*n* = 1937)	*p*
Age in years, Mdn (IQR)	54 (42-70)	63 (47-75)	<0.001
Age group			
<19 years	122 (4.1)	52 (2.7)	0.009
20–39 years	229 (17.8)	248 (12.8)	<0.001
40–59 years	1131 (38.2)	582 (30.0)	<0.001
60–79 years	909 (30.7)	730 (37.7)	<0.001
≥80 years	273 (9.2)	326 (16.8)	<0.001
Sex, women	1726 (58.2)	1137 (58.7)	0.728
LOS in days, Mdn (IQR)	12 (6-21)	11 (6-23)	0.878
Medical type of DRG (*n* = 4107)	2281 (89.0)	1381 (80.7)	<0.001
Complication, cellulitis	184 (6.2)	130 (6.7)	0.482
PG-related comorbidities			
IBD	451 (15.2)	319 (16.5)	0.239
Neoplasms	239 (8.1)	249 (12.9)	<0.001
Rheumatoid arthritis	152 (5.1)	102 (5.3)	0.830
Leukemia	72 (2.4)	97 (5.0)	<0.001
Stoma	94 (3.2)	71 (3,7)	0.373
MGUS	78 (2.6)	53 (2.7)	0.824
Hidradenitis suppurativa	85 (2.9)	37 (1.9)	0.035
Myelodysplastic syndrome	48 (1.6)	45 (2.3)	0,077
Lymphoma.	35 (1.2)	51 (2.6)	<0.001
Hepatitis C virus	41 (1.4)	40 (2.1)	0.067
Sweet syndrome	38 (1.3)	23 (1.2)	0.770
Behçet's disease	33 (1.1)	20 (1.0)	0.789
SpA	29 (1.0)	23 (1.9)	0.489
Unrelated comorbidities			
Hypertension	782 (26.4)	279 (37.6)	<0.001
Diabetes mellitus	516 (17.4)	430 (22.2)	<0.001
Dyslipidemia	384 (13.0)	327 (16.9)	<0.001
Chronis kidney disease	161 (5.4)	242 (12.5)	<0.001
Obesity	309 (7.1)	174 (9.0)	0.014
Atherosclerosis	69 (2,3)	94 (4.9)	<0.001
Peripheral vascular disease	24 (0.4)	25 (1.3)	0.098

TABLE 3 (Continued)

Abbreviations: DRG, diagnosis-related group; IBD, inflammatory bowel disease; IQR, interquartile range; LOS, length of hospital stay; Mdn, median; MGUS, monoclonal gammopathy of undetermined significance; ND, no data; PG, pyoderma gangrenosum; SpA, seronegative spondyloarthropathy.

TABLE 4 Risk factors I (epidemiological and clinical characteristics) in people admitted to hospital with pyoderma gangrenosum (1999–2021, Spain).

	n Deaths/total	(%)	OR (95% CI)	*p*	aOR (95% CI)	*p*
Sex						
Men	107/2039	5.2	1		1	
Women	168/2862	5.9	1.26 (0.87–1.44)	0.351	0.72 (0.66–1.38)	0.314
Age						
<19 years	1/174	0.6	1		1	
20–39 years	10/177	1.3	0.25 (0.28–17.2)	0.439	2.39 (0.30–18.2)	0.409
40–59 years	50/1713	2.9	5.21 (0.714–37.2)	0.104	4.84 (0.66–35.2)	0.121
60–79 years	128/1639	7.8	14.65 (2.03–105)	0.008	10.7 (1.46–78.2)	0.019
≥80 years	86/598	14.4	29.05 (4.01–210)	0.001	18.9 (2.6–139)	0.004
PG diagnosis						
Primary[a]	88/2964	3.0	1		1	
Secondary[b]	187/1937	9.7	3.25 (2.54–4.16)	<0.001	2.73 (2.09–3.79)	<0.001
IBD						
No	255/4131	6.2	1		1	
Yes	20/770	2.6	0.40 (0.25-0.64)	<0.001	0.75 (0.46–1.26)	0.251
RA						
No	261/4647	5.6	1		–	
Yes	14/254	5.5	0.98 (0.56–1.70)	0.915	–	
SpA						
No	275/4819	5.7	1		–	
Yes	0/52	0.0	NA	0.118	–	
MGUS						
No	270/4770	5.7	1		–	
Yes	5/131	3.8	0.66 (0.26–1.83)	0.367	–	
Sweet syndrome						
No	271/4870	5.6	1		–	
Yes	4/61	6.6%	1.18 (0.46–3.28)	0.753	–	
Stoma						
No	267/4736	5.6	1		–	
Yes	8/165	2.9	0.85 (0.41–1.75)	0.655	–	
HS						
No	269/4779	5.6	1		–	
Yes	6/122	4.9	0.86 (0.37–1.98)	0.571	–	
Behçet's disease						
No	273/4848	5.6	1		–	
Yes	2/53	3.8	0.65 (0.15–0.71)	0.715	–	
MDS						
No	260/4808	5.4	1		1	
Yes	15/793	16.1	3.65 (1.90–5.98)	<0.001	1.72 (0.92–3.22)	0.088

(Continues)

TABLE 4 (Continued)

	n Deaths/total	(%)	OR (95% CI)	*p*	aOR (95% CI)	*p*
Leukemia						
No	253/4732	5.3	1		1	
Yes	22/169	13.0	2.65 (1.63–4.22)	< 0.001	2.65 (1.61–4.33)	<0.001
Lymphoma						
No	266/4915	5.5	1		1	
Yes	9/88	10.5	1.99 (1.00–4.03)	0.048	1.62 (1.14–2.34)	0.156
Hepatitis C						
No	270/4820	5.6	1		–	
Yes	5/81	6.2	1.10 (0.44–2.78)	0.825	–	
Neoplasms						
No	222/4413	5.0	1		1	
Yes	53/488	10.9	2.30 (1.67–3.15)	<0.001	1.62 (1.11–2.30)	0.006

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; DRG, diagnosis-related group; HS, hidradenitis suppurativa; IBD, inflammatory bowel disease; MDS, myelodysplastic syndrome; MGUS, monoclonal gammopathy of undetermined significance; OR, odds ratio; RA, rheumatoid arthritis; SpA, seronegative spondyloarthropathy.

[a]Listed among the first three diagnoses.

[b]Listed in fourth to last position.

TABLE 5 Risk factors II (comorbidities unrelated to pyoderma gangrenosum [PG]) in people admitted to hospital with PG (1999–2021, Spain).

	n Deaths/total	(%)	OR (95% CI)	*p*	aOR (95% CI)	*p*
Hypertension						
No	159/3390	4.7	1		1	
Yes	116/1511	7.7	1.89 (1.31–2.16)	<0.001	0.88 (0.67–1.16)	0.378
Diabetes mellitus						
No	183/3955	4.6	1		1	
Yes	92/946	9.7	2.22 (1.71–2.88)	<0.001	1.61 (1.14–2.34)	0.001
Chronic kidney disease						
No	225/4498	5.0	1		1	
Yes	50/403	12.4	2.69 (1.94–3.74)	<0.001	1.41 (1.06–2.14)	0.002
Dyslipidemia						
No	234/4190	5.6			–	
Yes	41/711	5.8	1.03 (0.735–1.45)	0.561	–	
Atherosclerosis						
No	261/4738	5.5	1		–	
Yes	14/163	8.6	1.61 (0.91–2.82)	0.093	–	
Obesity						
No	255/4518	5.6	1		–	
Yes	20/383	5.2	0.92 (0.56–1.47)	0.730	–	
Peripheral vascular disease						
No	271/4852	5.6	1		–	
Yes	4/49	8.2	1.50 (0.53–4.02)	0.721	–	

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; OR: odds ratio.

TABLE 6 Economic burden of people admitted to hospital with PG (1999–2021, Spain).

Variable	Cost in EUR			p
	25th percentile	Median	75th percentile	
Age group				
0–20 years	2425.00	3237.05	4736.00	<0.001
19–39 years	2683.00	.232.00	4665.52	
40–59 years	2806.00	3606.00	5043.00	
60–79 years	3074.00	4079.20	5628.14	
≥80 years	3137.00	4085.00	5435.00	
Sex				
Men	2924.00	3809.36	5294.87	0.203
Women	2885.34	3738.00	5074.00	
Outcome				
Discharge	2850.99	3737.45	5043.00	<0.001
Death	4108.60	5419.00	8879.01	
Type of DRG (n = 4107)				
Medical	3009.44	3738.00	4734.00	<0.001
Surgical	5984.00	9001.50	13240.64	
PG diagnosis				
Primary[a]	2705.00	3264.00	4609.57	<0.001
Secondary[b]	3235.39	4483.11	6680.79	

Abbreviations: DRG, diagnosis-related group; PG, pyoderma gangrenosum.
[a]Listed among the first three diagnoses.
[b]Listed in fourth to last position.

colleagues carried out in the United Kingdom found that the risk of dying in people with PG (associated with IBD in 23% of cases) was 3.03 higher than in the general population, and 1.79 times higher than in a group of IBD patients without PG.[15]

We also analyzed the factors related to dying with PG, which included older age, leukemia, and neoplasms. Older age and hematological diseases are associated with higher death rates in people with other clinical entities, such as coronavirus disease 2019 (COVID-19).[16] However, in our study, the risk of dying in hospital was lower among people with IBD versus people without. We also found an association between mortality and conditions unrelated to PG, such as diabetes and chronic kidney disease, in line with other studies.[17,18]

The cost of admission for PG increased over the years, and was higher in people who died, in older people, and in those admitted for a surgical DRG. The same factors have been associated with higher costs in previous studies that evaluated other clinical entities in Spain[19,20] and in the European Union.[21]

One strength of our retrospective study is that it demonstrates the evolution of PG cases requiring hospitalization in Spain over 23 years. However, retrospective studies are helpful in generating hypotheses and showing trends, but they are by no means the best studies to investigate rare diseases that are challenging to diagnose.

The limitations of our study include those typically associated with the use of medico-administrative databases with coding rules. First, the HDR documents hospital admissions, and each admission (and readmission) is considered a new episode; therefore, some patients will have been included more than once. Second, the information available for each patient is the set of diagnoses coded at hospital discharge, and on some occasions, only the diagnoses considered most relevant by the attending clinician will be recorded. Diagnostic coding poses challenges when it comes to conditions lacking specific tests or pathologies for confirmation. Clinicians recording diagnostic codes in an uncontrolled manner can result in information that's hard to verify, impacting data accuracy and reliability. This lack of specificity can lead to both over and underdiagnosis of medical conditions. Additionally, when a condition is coded as a secondary diagnosis in nearly 40% of cases, it suggests it might not be the primary reason for the patient's admission and could be incidental to the main condition being treated. This underscores the importance of careful and precise diagnostic coding to ensure healthcare data accurately reflects patient conditions and treatment needs. Furthermore, coded diagnoses are not always used. Third, because this is a retrospective study, we had no opportunity to review patients' medical histories and check data for accuracy. Lastly, the HDR provides no data on medical as infusions of intravenous immunoglobulins or infliximab or surgical interventions received (as amputation) by the patients.

In conclusion, our study shows that PG cases in the inpatient setting in Spain over the past 23 years make up a tiny proportion of all hospital admissions, although the rate of hospitalization for PG has increased in the last two decades. Other factors that increased over the study period were patient age, the rates of PG-related comorbidities such as IBD, and the rates of unrelated comorbidities such as diabetes mellitus, high blood pressure, and chronic kidney disease. The risk of death was greater in people who had PG as a primary diagnosis on admission, older people, and people with leukemia, neoplasms, diabetes mellitus, or chronic kidney disease.

Data recorded in a national medico-administrative database (HDR) provides key information on the burden of PG in Spain. The present study highlights the burden of PG, PG-related comorbidities, and risk factors for death and high costs. Analyses of this type are valuable for documenting the burden of PG by comorbidity.

AUTHOR CONTRIBUTIONS

Isabel Belinchón-Romero: Conceptualization; investigation; writing—original draft; writing—review and editing. **Verónica Sánchez-Martínez**: Data curation; formal analysis; investigation; writing—review and editing. **Clara Ramos-Belinchón**: Data curation; formal analysis; writing—review and editing. **José-Manuel Ramos-Rincón**: Conceptualization; data curation; formal analysis; investigation; writing—original draft; writing—review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

TRANSPARENCY STATEMENT

The lead author José-Manuel Ramos-Rincón affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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