

# Features and Associated Factors of Bacterial Skin Infections in Hospitalized Patients with Pemphigus: A Single-Center Retrospective Study

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## Research

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# Abstract

**Background:** Infections were the primary cause of death (34.3%-55.5%) in patients with pemphigus. Skin was usually the origin of infections. The study aimed to explore features and associated factors of bacterial skin infections (BSIs) in inpatients with pemphigus.

**Methods:** One hundred and eighty-four inpatients with pemphigus visiting the dermatology department of Peking University First hospital during 2013 to 2019 were continuously recruited to study the characteristics and associated factors of BSIs.

**Results:** Of patients enrolled, pemphigus vulgaris (PV, n=142) and pemphigus foliaceus (PF, n=9) were most common, followed by pemphigus erythematosus (PE, n=25) and pemphigus vegetans (Pveg, n=1). Eighty-seven of 177 (49.2%) inpatients developed BSIs, and they had a longer length of stay compared with inpatients without BSIs (median: 18.9 days vs. 14.1 days,  $p = 0.008$ ). *Staphylococcus aureus* was the most common bacteria and highly resistant to penicillin (91.9%). Higher levels of anti-Dsg1 autoantibodies ( $>124.2\text{U/mL}$ ) ( $p < 0.001$ , odds ratio [OR]=3.564, 95% confidence interval [CI]: 1.784-7.123) and anti-Dsg3 autoantibodies ( $>169.5\text{U/mL}$ ) ( $p = 0.03$ , OR=1.074, 95% CI: 1.084-3.969) were underlying risk factors of BSIs. As for Gram's stain of bacteria, females had a lower rate of Gram-positive infections ( $p = 0.03$ ). Patients systematically using of antibiotics ( $p = 0.05$ ) had a higher rate of Gram-negative infections. Inpatients with history of hospitalization had a higher rate of Gram-negative and co-infections ( $p = 0.03$ ).

**Conclusions:** Inpatients with pemphigus had a high incidence rate of BSIs. High levels of anti-Dsg1 ( $>124.2\text{U/mL}$ ) and Dsg3 autoantibodies ( $>169.5\text{U/mL}$ ) might be underlying risk factors for BSIs.

## Introduction

Pemphigus is an autoimmune bullous disease characterized by flaccid blisters and erosions of skin/mucous membranes [1]. Annual incidence varies from 0.76 to 16.1 cases per million [2, 3]. Subtypes of pemphigus were differentiated by clinical features, histopathology, and specific autoantibodies [2]. Pemphigus vulgaris (PV) (65%) and pemphigus foliaceus (PF) (23%) are the most frequent subtypes [4]. Though the use of glucocorticoids and immunosuppressive agents has significantly diminished the mortality, the prognosis of pemphigus is still worse than that of general population [2]. Infections are the most frequent complications of patients with pemphigus and account for 34.3%-55.5% of all death [5–8]. Besides, inpatients with pemphigus have a higher rate of serious infections than inpatients without a diagnosis of autoimmune bullous disease (50.4% vs. 25.4%) [9]. In pemphigus with serious infections, hospital expenses increases, and length of stay (LOS) extends [9]. Skin is usually the origin of infections [10]. Fragile barrier, dysfunction of immunity, and usage of systemic corticosteroids and/or other immunosuppressing agents may be the causes [5–8]. Therefore, the study aims to explore the features and associated factors for bacterial skin infections (BSIs), which may be helpful for the control of BSIs.

# Materials And Methods

## Patients and data collection

This was a retrospective study conducted at Peking University First Hospital. The study followed the Declaration of Helsinki and was approved by the ethics committee of the hospital. One hundred and seventy-seven inpatients with pemphigus were continuously recruited from November 2014 to April 2019. Diagnostic criteria of pemphigus included: (1) flaccid blisters and erosions on skin or mucosa, (2) suprabasal/subcorneal loss of epidermal adhesion in histopathology, (3) IgG and/or C3 deposits on the surface of keratinocytes, and (4) seropositivity of anti-Dsg1 and/or anti-Dsg3 autoantibodies (MBL, Nagoya, Japan) [11]. Bacterial skin infections (BSIs) were diagnosed by purulent skin secretions, fever, elevated inflammatory markers (white cells, neutrophils, C-reactive protein, etc.), and culture of skin swab. A culture of skin swab was necessary for the diagnosis of BSIs. If the isolated bacteria might be contaminated colonized, clinical features and other laboratory examinations would be thoroughly considered for the determination of BSIs. BSIs identified within the first 48 hours was identified as community-acquired infections [12]. Body mass index (BMI) more than 28 kg/m<sup>2</sup> was defined as obesity [13]. Hypoalbuminemia was defined as < 30 g/L [14].

Demographic characteristics, history of previous hospitalization, the severity of skin lesions, and levels of autoantibodies were recorded. The treatment protocols within 2 weeks before this hospitalization were also collected. The severity of skin lesions graded as follows: mild, < 10.0% body surface area (BSA); moderate, 10.0%-30.0% BSA; severe, 30.0%-50.0% BSA; extensive, ≥ 50.0% BSA. The systemic glucocorticoids was graded as follows (equivalent to prednisone): low dosage: < 0.5 mg/(kgžd); medium dosage: ≥ 0.5 mg/(kgžd) and < 1.0 mg/(kgžd); high dosage ≥ 1.0 mg/(kgžd).

## Statistical analysis

Data were analyzed with IBM SPSS 24.0 (IBM Corp, Armonk, NY). Continuous variables were converted into categorical variables by the Receiver Operating Characteristics curve, by which anti-Dsg1 and anti-Dsg3 autoantibodies were grouped by 124.2 IU/ml and 169.5 IU/ml, respectively, and age was grouped by 53.5 years. Non-parametric tests were used for variables not meeting the normal distribution. Chi-square test or Fisher's exact test were used for variables with normal distribution. Factors with  $P \leq 0.10$  were reanalyzed by binary regression analysis.  $P < 0.05$  was considered statistically significant. See Fig. 1 for the study and analysis flow chart.

## Results

### Clinical features

A total number of 177 inpatients were enrolled, including PV (80.2%, 142/177), pemphigus erythematosus (PE) (14.1%, 25/177), PF (5.1%, 9/177), and pemphigus vegetans (Pveg) (0.6%, 1/177). The median age was 50.4 years (range: 14–80 years), and the female/male ratio was 0.90. The incidence of diabetes

mellitus (DM) (18.6%, 33/177), hypertension (27.7%, 49 /177), and osteoporosis (11.3%, 20/184) were high. Twelve (6.8%), 31 (17.5%), 52 (29.4%) and 82 (46.3%) of 177 patients had mild, moderate, severe and extensive skin lesions, respectively. Most inpatients (70.6%, 125/177) received oral corticosteroids, and 114 (91.2%) of 125 had detailed records of the dosage. Of them, 43.9% (50/114) patients took medium dose (0.5 mg/kg·d -1.0 mg/kg·d), and 24.6% (28/114) patients took high dose ( $\geq 1.0$  mg/kg·d) of prednisone or the equivalent. Eighty-seven of 177 (49.2%) inpatients developed BSIs. LOS was analyzed by a non-parametric test, and inpatients with BSIs had longer LOS compared with inpatients without BSIs (median: 18.9 days vs. 14.1 days,  $p = 0.008$ ).

## Bacterial Spectrum And Drug Resistance

Eighty-seven of 177 (49.2%) patients developed BSIs, and 17 of 87 (19.5%) inpatients isolated more than one type of bacteria. If a patient had the isolation of *Staphylococcus aureus*, *S. haemolyticus*, and *S. epidermidis*, it was hard to differentiate whether the *S. epidermidis* was contaminated or not. Therefore, we showed all isolated bacteria of the inpatients definitely diagnosed as BSIs. The Bacterial spectrum of all inpatients with BSIs was presented in Fig. 2. Sixty-two (71.3%, 62/87) inpatients were infected with *S. aureus*, followed by *Escherichia coli* (8.0%, 7/87), and *Methicillin-resistant coagulase negative staphylococcus* (8.0%, 7/87). Eighty-one (93.1%, 81/87) inpatients presented with community-acquired infections. Patients with hospital-acquired infections had a higher incidence of *S. aureus* (83.3%, 5/6). The bacterial spectrum of community-acquired infections and hospital-acquired infection infections was illustrated in Fig. 3.

As for the drug resistance of *S. aureus*, penicillin G (91.9%, 57/62), erythromycin (75.8%, 47/62), and clindamycin (45.2%, 28/62) had the highest resistance rate. The resistance rate of rifampicin (1.6%, 1/62), linezolid (1.6%, 1/62), quinupristin (1.6%, 1/62), and tigecycline (1.6%, 1/62) was the lowest. All patients kept sensitive to vancomycin (Fig. 4). As the second most common bacteria, *Methicillin-resistant coagulase negative staphylococcus* was also highly resistant to penicillin (100.0%, 7/7) and erythromycin (100.0%, 7/7). *Methicillin-resistant coagulase negative staphylococcus* remained 100% sensitive to tigecycline and vancomycin.

## Risk Factors For Bsis

Sex ( $p = 0.49$ ), age ( $p = 0.96$ ), obesity ( $p = 0.24$ ), and smoke ( $p = 0.13$ ) did not significantly associate with BSIs. Cerebrovascular disease (CVD) ( $p = 0.96$ ), chronic heart disease (CHD) ( $p = 0.34$ ), diabetes mellitus (DM) ( $p = 0.28$ ), hypertension ( $p = 0.72$ ), and osteoporosis ( $p = 0.58$ ), did not associate with higher incidence of BSIs. Similarly, severity of skin lesions ( $p = 0.08$ ), subtype of pemphigus ( $p = 0.51$ ), and hypoalbuminemia ( $p = 0.09$ ) were not underlying risk factors for BSIs. Higher levels of anti-Dsg1 autoantibodies ( $> 124.2\text{U/mL}$ ) ( $p < 0.001$ ) and anti-Dsg3 autoantibodies ( $> 169.5\text{U/mL}$ ) ( $p = 0.01$ ) were associated with BSIs (Table 1). The variables with  $p \leq 0.10$  were reanalyzed by binary regression analysis and the results showed in Table 2. Higher levels of anti-Dsg1 autoantibodies ( $> 124.2\text{U/mL}$ ) ( $p < 0.001$ ,

odds ratio [OR] = 3.564, 95% CI: 1.784–7.123) and anti-Dsg3 autoantibodies (> 169.5U/mL) ( $p = 0.03$ , OR = 2.074, 95% CI: 1.084–3.969) were strongly associated with BSIs.

## Associated Factors For The Type Of Bacteria

In inpatients with BSIs, 60 (69.0%, 60/87), 13 (14.9%, 13/87), and 14 (16.1%, 14/87) had infections of Gram-positive bacteria, Gram-negative bacteria and coinfection, respectively. Females had a higher rate of coinfection (54.3% vs. 35.7%) and a lower rate of Gram-negative infection (25.4% vs. 84.6%) compared to males ( $p = 0.03$ ). Though the result was not significantly different ( $p = 0.37$ ), a higher rate of coinfection was observed in patients < 53.5 years compared to  $\geq 53.5$  years' (71.4% vs. 28.6%). Comorbidities, including CVD ( $p = 0.72$ ), CHD ( $p = 0.72$ ), DM ( $p = 0.39$ ), hypertension ( $p = 0.86$ ), and osteoporosis ( $p = 0.92$ ), were not associated with Gram's stain. Bedridden was not significantly associated with Gram's stain ( $p = 0.09$ ). Within 2 weeks before this admission, patients taking oral antibiotics had a higher rate of Gram-negative isolation ( $p = 0.05$ ). Patients with previous hospitalization had higher rates of Gram-negative infection and co-infections ( $p = 0.03$ ) (Table 3).

## Discussion/conclusion

Infection was the most common comorbidity in patients with pemphigus [9, 15], and increased hospital expenses and LOS [9]. Our study also found the LOS prolonged in inpatients with BSIs ( $p = 0.008$ ). Ninety-four (49.2%, 87/177) inpatients with pemphigus developed BSIs in our research, parallel with another study (52%, 73/141) [16]. *S. aureus* was the most common type of bacteria [10, 17–19]. The drug resistance of *S. aureus* was striking [17]. *S. aureus* was highly resistant to penicillin (91.9%), erythromycin (75.8%), and clindamycin (45.2%). *S. aureus* was sensitive to vancomycin and moxifloxacin, which might be good choices for inpatients who need empirical and vigorous treatment.

Associated factors for BSIs were explored. Hsu et al. suggested that patients who had multi-morbidities and poor health conditions were more likely to develop lethal infections [15], and DM was associated with infections in many studies [1, 16, 17, 20]. However, comorbidities, such as DM, CVD, CHD, etc., were not significantly associated with BSIs in our study. Hypoalbuminemia was suggested to be associated with poor health conditions and had a higher rate of BSIs in previous studies [21, 22], but no association was observed in our analysis.

Many studies linked infections to immunosuppressive agents [23, 24]. Hsu et al. proposed that infection in patients with pemphigus was iatrogenic. The role of glucocorticoids and other immunosuppressive agents of infection was uncertain [15]. Glucocorticoids and immunosuppressive agents were not significantly associated with BSIs in our studies. It might be due to the influences of both immunosuppression and promoting recovery of skin lesions of these drugs. Although 82 of 177 (46.3%) patients had extensive, only 43 of 177 (24.3%) patients accepted immunosuppressors before his hospitalization. The nonstandard treatment also influenced the association between immunosuppressors and BSIs.

Higher levels of anti-Dsg1 autoantibodies ( $> 124.2\text{U/mL}$ ) ( $p < 0.001$ ) and anti-Dsg3 autoantibodies ( $> 169.5\text{U/mL}$ ) ( $p = 0.03$ ) were significantly associated with BSIs. Patients with high levels of anti-Dsg1 autoantibodies or higher anti-Dsg3 autoantibodies had high disease activity and severe or even recalcitrant skin lesions [25–27], which could explain the phenomena. However, the association between the area of skin lesions and BSIs was not significant ( $p = 0.08$ ) in our study, which might be because we only briefly calculated the area of skin lesions and did not consider the types of skin damage for the incomplete record.

We also paid attention to the associated factors of the type of bacteria. Female had higher incidence of coinfection (64.3% vs. 35.7%), and lower incidence of Gram-negative infection (15.4% vs. 84.6%) ( $p = 0.03$ ) compared to males in our study. Different gender-related lifestyle and physical function might cause this difference [28–30]. The discrepancy of body-size, immune capacity, and energy availability between males and females might be the underlying reasons. Besides, Thompson et al. found that pathogen transmission and virulence were much higher in females [31]. Anyway, the underlying interesting mechanism of different infections in different gender was unclear and needed further studies. The use of systemic antibiotics was associated with a higher rate of Gram-negative infections. Dysbacteriosis induced by antibiotics might be the reason [32]. Previous hospitalization ( $p = 0.03$ ) had a higher rate of Gram-negative infection and co-infections. It was known that the bacteria spectrum of the hospital was different from the community. For example, the most common bacteria of community-acquired pneumonia was *Streptococcus pneumoniae*, while the most common bacteria of hospital-acquired pneumonia was *Acinetobacter baumannii*, and *Pseudomonas aeruginosa* [33, 34]. Iatrogenic manipulation and the use of antibiotics caused the difference of bacterial spectrum [35, 36]. So we should pay more attention to the infections of Gram-negative bacteria in inpatients with a history of previous hospitalization.

The study has some limitations. This is a retrospective study in a single center, so the generalizability might be influenced, and selection bias existed. This study did not enroll outpatients with pemphigus, which might influence the spectrum of bacteria and drug resistance. The relatively small sample size was also a disadvantage of this study. Patients admitted to the tertiary hospital might be more serious, so the incidence of BSIs might be overestimated. Finally, the authors did not exclude the colonized or contaminated bacteria in showing the species of isolated bacteria. Though the limitations exist, the results proposed in the study are beneficial to understand the BSIs and may be the basis for high-quality researches in the future.

The study found that inpatients with pemphigus had a high incidence rate of BSIs, and *S. aureus* was the most common isolated bacteria. High levels of anti-Dsg1 ( $> 124.2\text{U/mL}$ ) and Dsg3 autoantibodies ( $> 169.5\text{U/mL}$ ) might be underlying risk factors for BSIs. Besides, gender, systemic usage of antibiotics, and history of hospitalization might influence the type of isolated bacteria. We highlighted the importance of further exploration of underlying risk factors of BSIs in inpatients with pemphigus.

## Abbreviations

AIBD

autoimmune bullous disease; BMI:body mass index; BSA:body surface area; BSIs:bacterial skin infections; CHD:chronic heart disease; CI:confidence interval; CVD:cerebrovascular disease; DM:diabetes mellitus; LOS:length of stay; OR:odd ratio; PE:pemphigus erythematosus; PF:pemphigus foliaceus; PV:pemphigus vulgaris; Pveg:pemphigus vegetans.

## Declarations

- The study was approved by the ethics committee of Peking University First Hospital.
- All the authors were active participants: FL and YW were responsible for data collection and management, statistical analysis and interpretation, literature research, and manuscript writing; WB, XZ, and XC were responsible for data collection, statistical analysis, and interpretation; MW was responsible for the design of the study, statistical analysis and interpretation, and revision of the paper. All authors read and approved the final manuscript.
- The datasets of current study are available from the corresponding author on reasonable request.
- The authors declare that they have no competing interests.
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- We wish to submit the manuscript for publication in *Annals of Clinical Microbiology and Antimicrobials*<sup>®</sup>, and the manuscript is not currently under consideration for publication in another journal.

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# Tables

Table 1  
Associated factors of BSIs by univariate analysis.

Features	Without BSIs (n = 90)	BSIs (n = 87)	P-value
Sex			0.49
Female (n = 84)	45 (50.0)	39 (44.8)	
Male (n = 93)	45 (50.0)	48 (55.2)	
Age			0.96
<53.5 years (n = 100)	51 (56.7)	49 (56.3)	
≥53.5 years (n = 77)	39 (43.3)	38 (43.7)	
Obesity (n = 25) <sup>1</sup>	10 (11.4)	15 (17.6)	0.24
Smoke (n = 16)	11 (12.2)	5 (5.7)	0.13
Alcohol intake (n = 11)	8 (8.9)	3 (3.4)	0.13
Comorbidities			
CVD (n = 7)	3 (3.3)	4 (4.6)	0.96
CHD (n = 5)	1 (1.1)	4 (4.6)	0.34
Diabetes mellitus (n = 33)	14 (15.6)	19 (21.8)	0.28
Hypertension (n = 49)	26 (28.9)	23(26.4)	0.72
Osteoporosis (n = 20)	9 (10.0)	11 (12.6)	0.58
Bedridden (n = 2)	0 (0.0)	2 (2.3)	0.24
Previous hospitalization (n = 18)	10 (11.1)	8 (9.2)	0.67
Severity of skin lesions	9 (10.0)	3 (3.4)	0.08
Mild (n = 12)	20 (22.2)	11 (12.6)	
Moderate (n = 31)	24 (26.7)	28 (32.2)	
Severe (n = 52)	37 (41.1)	45 (51.7)	
Extensive (n = 82)			
Subtype of pemphigus			0.51
<sup>1</sup> Four patients (without BSIs = 2, BSIs = 2) had no records of BMI so that these patients could not be assessed for obesity.			
<sup>2</sup> Seven patients had no records of levels of anti-dsg1 autoantibodies (without BSIs = 3, BSIs = 4).			
<sup>3</sup> Seven patients had no records of levels of anti-dsg3 autoantibodies (without BSIs = 3, BSIs = 4).			
Abbreviations: CVD, cerebrovascular disease; CHD, coronary heart disease; PV, Pemphigus vulgaris; PVeg, pemphigus vegetans; PE, pemphigus erythematosus; PF, pemphigus foliaceus; Dsg, desmoglein; BSIs, bacterial skin infections; BMI, body mass index.			

Features	Without BSIs (n = 90)	BSIs (n = 87)	P-value
PV and PVeg (n = 143)	71 (78.9)	72 (82.8)	
PE and PF (n = 34)	19 (21.1)	15 (17.2)	
Therapy			
Antibiotics (n = 40)	20 (22.2)	20 (23.0)	0.90
Glucocorticoids (n = 129)	65 (72.2)	64 (73.6)	0.84
Immunosuppressive agent (n = 43)	26 (28.9)	17 (19.5)	0.15
Hypoalbuminemia (n = 21)	7 (8.0)	14 (16.3)	0.09
Anti-dsg1 autoantibodies <sup>2</sup>			< 0.001
≤ 124.2 IU/ml (n = 61)	44 (50.6)	17 (20.5)	
> 124.2 IU/ml (n = 109)	43 (49.4)	66 (79.5)	
Anti-dsg3 autoantibodies <sup>3</sup>			0.01
≤169.5 IU/ml (n = 93)	56 (64.4)	37 (44.6)	
>169.5 IU/ml (n = 77)	31 (35.6)	46 (55.4)	
<sup>1</sup> Four patients (without BSIs = 2, BSIs = 2) had no records of BMI so that these patients could not be assessed for obesity.			
<sup>2</sup> Seven patients had no records of levels of anti-dsg1 autoantibodies (without BSIs = 3, BSIs = 4).			
<sup>3</sup> Seven patients had no records of levels of anti-dsg3 autoantibodies (without BSIs = 3, BSIs = 4).			
Abbreviations: CVD, cerebrovascular disease; CHD, coronary heart disease; PV, Pemphigus vulgaris; PVeg, pemphigus vegetans; PE, pemphigus erythematosus; PF, pemphigus foliaceus; Dsg, desmoglein; BSIs, bacterial skin infections; BMI, body mass index.			

Table 2  
Associated factors of BSIs by binary regression analysis.

<b>Variables</b>	<b>OR (95% CI)</b>	<b>P-value</b>
Anti-Dsg1 autoantibodies		< 0.001
≤124.2 IU/mL	1.00	
>124.2 IU/mL	3.564 (1.784–7.123)	
Anti-Dsg3 autoantibodies		0.03
≤169.5	1.00	
>169.5	2.074 (1.084–3.969)	
Abbreviations: BSIs, bacterial skin infections; Dsg, desmoglein; OR, odds ratio; CI, confidence interval;		

Table 3

Associated factors of Gram stain of bacteria in patients with pemphigus by univariate analysis.

Features	Gram-positive (n = 60, %)	Gram-negative (n = 13, %)	Coinfection (n = 14, %)	P-value
Sex				0.03
Female (n = 39)	28 (46.7) <sup>a, b</sup>	2 (15.4) <sup>b</sup>	9 (64.3) <sup>a</sup>	
Male (n = 48)	35 (54.7) <sup>a, b</sup>	11 (84.6) <sup>b</sup>	5 (35.7) <sup>a</sup>	
Age				
<53.5 years (n = 49)	31 (51.7)	8 (61.5)	10 (71.4)	0.37
≥53.5 years (n = 38)	29 (48.3)	5 (38.5)	4 (28.6)	
Obesity (n = 15) <sup>1</sup>	8 (13.3)	5 (41.7)	2 (15.4)	0.10
Smoke (n = 5)	5 (8.3)	0 (0.0)	0 (0.0)	0.15
Alcohol intake (n = 3)	2 (3.3)	1 (7.7)	0 (0.0)	0.47
Comorbidities				
CVD (n = 4)	2 (3.3)	1 (7.7)	1 (7.1)	0.72
CHD (n = 4)	2 (3.3)	1 (7.7)	1 (7.1)	0.72
Diabetes mellitus (n = 19)	11 (18.3)	3 (23.1)	5 (35.7)	0.39
Hypertension (n = 23)	16 (26.7)	4 (30.8)	3 (21.4)	0.86
Osteoporosis (n = 11)	7 (11.7)	2 (15.4)	2 (14.3)	0.92
Bedridden (n = 2)	0 (0.0)	1 (7.7)	1 (7.1)	0.09
Previous hospitalization (n = 8)	2 (3.3) <sup>a</sup>	3 (23.1) <sup>b</sup>	3 (21.4) <sup>b</sup>	0.03
Severity of skin lesions				0.40
<sup>1</sup> Two patients (Gram-positive = 0, Gram-negative = 1, Coinfection = 1) had no records of body mass index so that these patients could not be assessed for obesity.				
<sup>2</sup> Four patients had no records of levels of anti-dsg1 autoantibodies (Gram-positive = 4, Gram-negative = 0, Coinfection = 0).				
<sup>3</sup> Four patients had no records of levels of anti-dsg3 autoantibodies (Gram-positive = 4, Gram-negative = 0, Coinfection = 0).				
Abbreviations: CVD, cerebrovascular disease; CHD, coronary heart disease; PV, Pemphigus vulgaris; PVeg, pemphigus vegetans; PE, pemphigus erythematosus; PF, pemphigus foliaceus; Dsg, desmoglein.				

Features	Gram-positive (n = 60, %)	Gram-negative (n = 13, %)	Coinfection (n = 14, %)	P-value
Mild (n = 3)	1 (1.7)	1 (7.7)	1 (7.1)	
Moderate (n = 11)	7 (11.7)	3 (23.1)	1 (7.1)	
Severe (n = 28)	17 (28.3)	4 (30.8)	7 (50.0)	
Extensive (n = 45)	35 (58.3)	5 (38.5)	5 (35.7)	
Subtype of pemphigus				0.92
PV and PVeg (n = 72)	49 (81.7)	11 (84.6)	12 (85.7)	
PE and PF (n = 15)	11 (18.3)	2 (15.4)	2 (14.3)	
Therapy				
Topical antibiotics (n = 10)	5 (8.3)	3 (23.1)	2 (14.3)	0.35
Systemic antibiotics (n = 11)	4 (6.7) <sup>a</sup>	4 (30.8) <sup>b</sup>	3 (21.4) <sup>a, b</sup>	0.05
Topical glucocorticoids (n = 7)	6 (10.0)	1 (7.7)	0 (0.0)	0.27
Systemic glucocorticoids (n = 62)	40 (66.7)	10 (76.9)	12 (85.7)	0.29
Immunosuppressive agents (n = 17)	13 (21.7)	2 (15.4)	2 (14.3)	0.75
Hypoalbuminemia (n = 14)	8 (13.6)	3 (23.1)	3 (21.4)	0.61
Anti-Dsg1 autoantibodies <sup>2</sup>				0.29
≤ 124.2 IU/mL (n = 17)	9 (16.1)	3 (23.1)	5 (35.7)	
> 124.2 IU/mL (n = 66)	47 (83.9)	10 (76.9)	9 (64.3)	
Anti-Dsg3 autoantibodies <sup>3</sup>				0.77

<sup>1</sup> Two patients (Gram-positive = 0, Gram-negative = 1, Coinfection = 1) had no records of body mass index so that these patients could not be assessed for obesity.

<sup>2</sup> Four patients had no records of levels of anti-dsg1 autoantibodies (Gram-positive = 4, Gram-negative = 0, Coinfection = 0).

<sup>3</sup> Four patients had no records of levels of anti-dsg3 autoantibodies (Gram-positive = 4, Gram-negative = 0, Coinfection = 0).

Abbreviations: CVD, cerebrovascular disease; CHD, coronary heart disease; PV, Pemphigus vulgaris; PVeg, pemphigus vegetans; PE, pemphigus erythematosus; PF, pemphigus foliaceus; Dsg, desmoglein.

Features	Gram-positive (n = 60, %)	Gram-negative (n = 13, %)	Coinfection (n = 14, %)	P-value
≤169.5 IU/mL (n = 37)	26 (46.4)	6 (46.2)	5 (35.7)	
> 169.5 IU/mL (n = 46)	30 (53.6)	7 (53.8)	9 (64.3)	
<sup>1</sup> Two patients (Gram-positive = 0, Gram-negative = 1, Coinfection = 1) had no records of body mass index so that these patients could not be assessed for obesity.				
<sup>2</sup> Four patients had no records of levels of anti-dsg1 autoantibodies (Gram-positive = 4, Gram-negative = 0, Coinfection = 0).				
<sup>3</sup> Four patients had no records of levels of anti-dsg3 autoantibodies (Gram-positive = 4, Gram-negative = 0, Coinfection = 0).				
Abbreviations: CVD, cerebrovascular disease; CHD, coronary heart disease; PV, Pemphigus vulgaris; PVeg, pemphigus vegetans; PE, pemphigus erythematosus; PF, pemphigus foliaceus; Dsg, desmoglein.				

## Figures

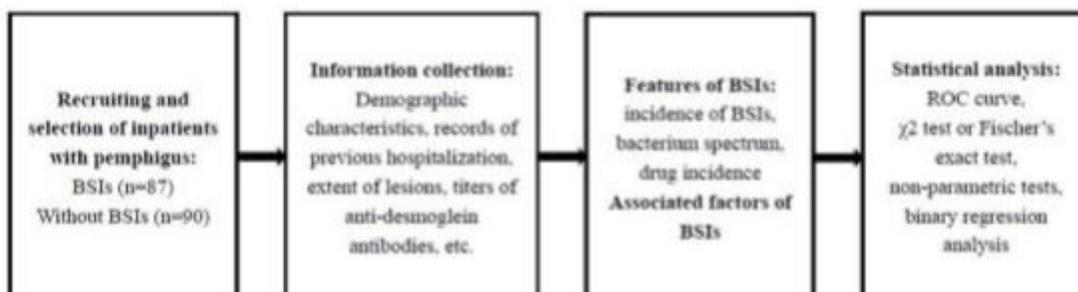
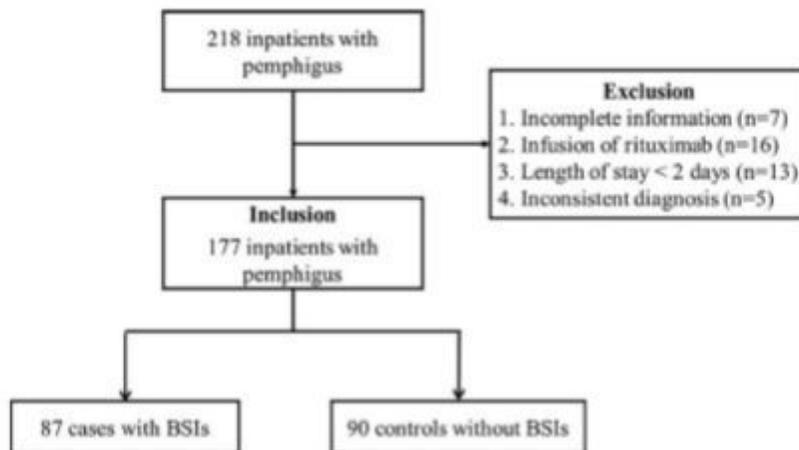


Figure 1

Flow diagram of the study.

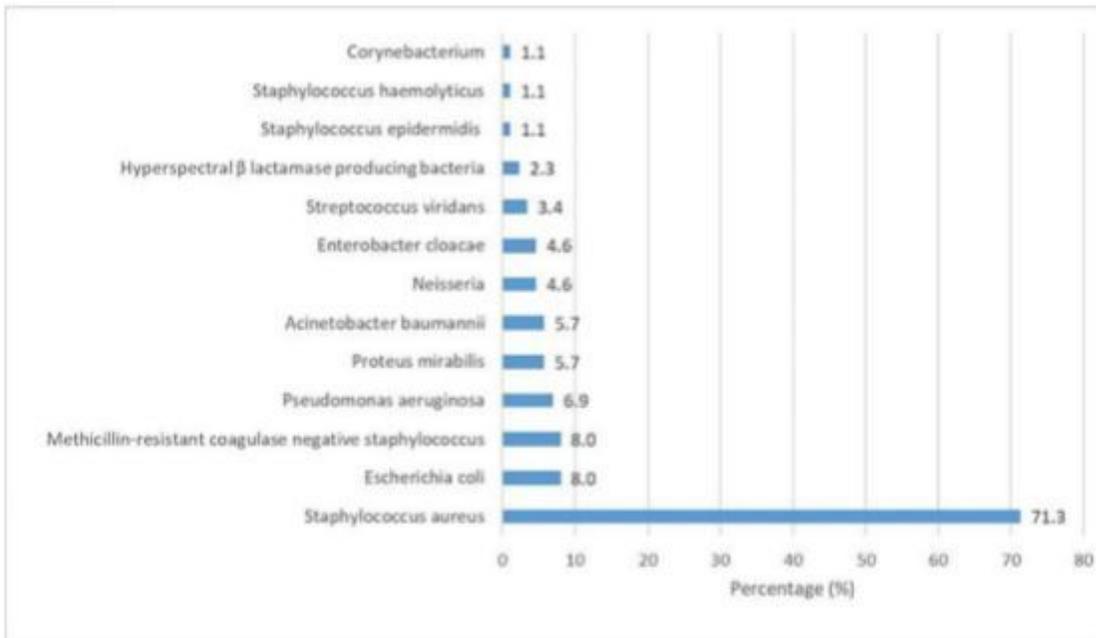
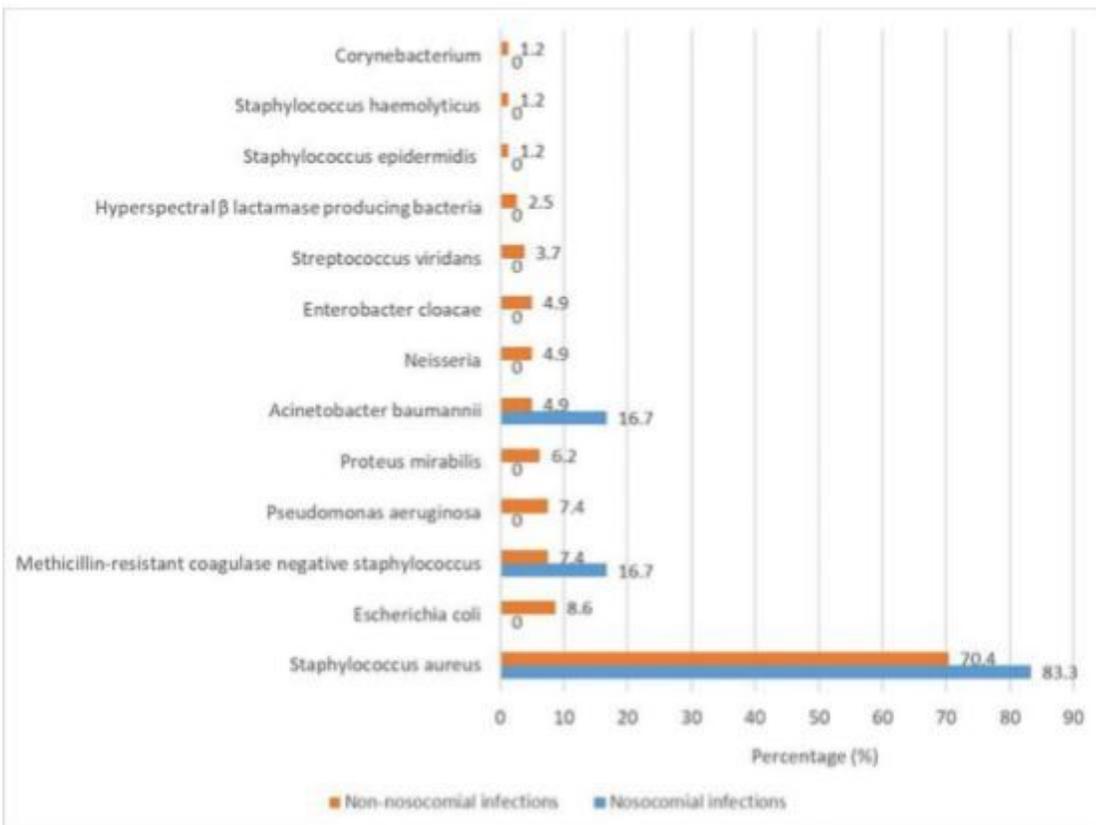


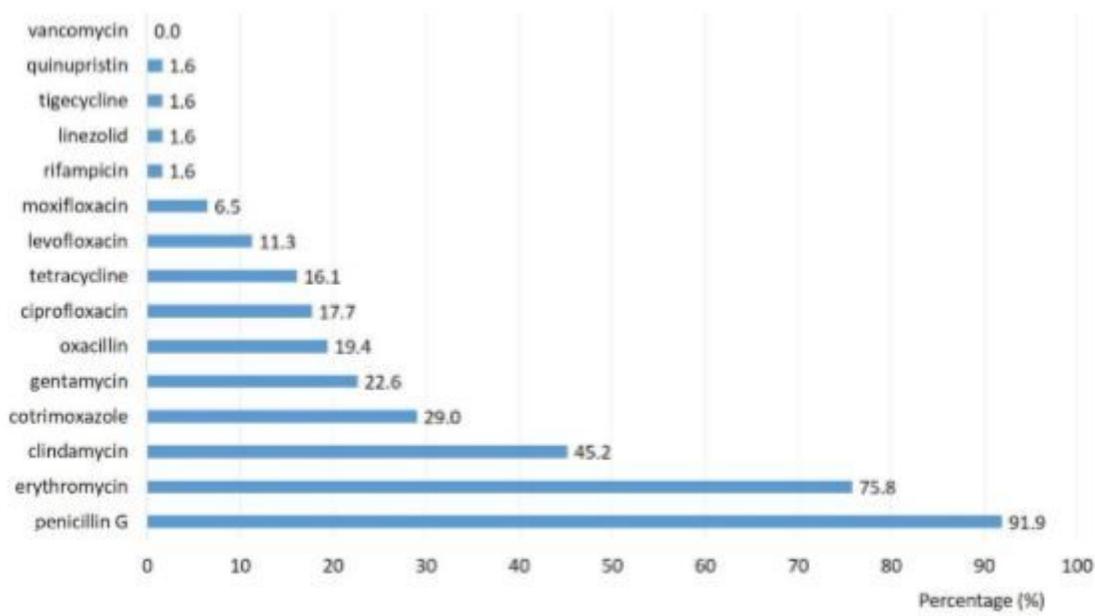
Figure 2

Bacteria spectrum of inpatients with pemphigus.



**Figure 3**

Bacteria spectrum of community-acquired infections and hospital-acquired (nosocomial) infections.



**Figure 4**

Drug resistance of *Staphylococcus aureus*.