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Article

Factors Associated with Candidiasis in Pemphigus Vulgaris Patients: Results from a Retrospective Study in Two Second-Care Hospitals in Mexico

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Abstract: Background: Infections are a major cause of morbidity and mortality in patients with pemphigus vulgaris (PV). One of the most common infections in these patients is candidiasis. This is probably due to the use of systemic immunosuppressant, including oral and intravenous corticosteroids, mainly in megadoses (pulse therapy), although it is unknown if there are other associated factors in addition to immunosuppressive treatment. We determine the factors associated with candidiasis in PV patients in two Second-Care hospitals in Mexico. Methods: We reviewed 100 cases with PV. Cases were randomly selected from the databases of two second-care hospitals between January 2010 and December 2019 (10 years). The primary endpoint was the incidence of candidiasis in patients with PV. Results: One hundred patients with PV were enrolled in this retrospective study. Candidiasis was observed in 79 patients (79%). A maximum corticosteroid dose of 55 mg/day during the last year ($p = 0.001$) and higher neutrophil/lymphocyte ratio were associated with candidiasis in patients with PV ($p = 0.001$). Conclusion: Risk factors favoring candidiasis in patients with PV are not only related to the use of corticosteroids, but also to demographic factors, the activity of the disease, and the systemic inflammation associated with autoimmunity.

Keywords: pemphigus vulgaris; neutrophil-lymphocyte ratio; platelet-neutrophil ratio; corticosteroids; candidiasis; candidemia

1. Introduction

Pemphigus vulgaris (PV) is an autoimmune disease associated with significant morbidity and mortality, and treatment with high-dose corticosteroids may increase the risk of infection, including candidiasis [1,2]. Systemic steroids can cause a variety of physical and mental health problems, including decreased bone density, cataracts, water and electrolyte imbalances, peptic ulcers, pancreatic inflammation, mental illness, diabetes, Cushing's syndrome, and opportunistic infections. Pathogens such as *Candida* usually coexist with other microorganisms in the skin microbiota and do not cause disease, but immunosuppressive conditions can promote their excessive growth, resulting in clinical manifestations. *Candida* species may contribute to the development of mucocutaneous infections, endocarditis, intravascular catheter infections, osteoarticular infections, and meningitis, which can ultimately be fatal if inadequately treated; prompt and effective treatment of such infections is essential to prevent serious complications.

Candidiasis may be more common in immunocompromised individuals, while in immunocompetent patients, the use of broad-spectrum antibiotics, immunosuppressive agents, chemotherapy, intravenous catheters, parenteral nutrition, surgery, malignancy, diabetes, and other factors may contribute to the incidence of candidiasis. Candidiasis is prevalent in patients with PV [1]. Treatment of PV often requires high-dose systemic steroids and adjuvant steroid-sparing drugs such as azathioprine or mycophenolate mofetil [3], which are valuable in effectively reducing recurrence rates when systemic steroids are tapered or withdrawn [4]. High-dose steroids in pulse therapy or rituximab are used in cases of inadequate response to standard treatment or in relapse

(appearance of at least 3 new lesions within 1 month that do not resolve within 1 week without treatment, or worsening of pre-existing lesions in a patient with controlled disease) [5,6]. Remission during treatment is characterized by the absence of new or existing lesions while the patient is receiving minimal therapy [6]. The duration of remission varies among patients, and in some cases, remission lasts longer. Patients may develop infections that complicate disease course, regardless of their phase of activity, relapse or remission [7,8]. Early detection of these infections can lead to effective treatment regimens. Candidiasis incidence varies with steroid dose and duration of use, but the specific steroid dose required to induce candidiasis remains unclear. Previous studies in patients with systemic lupus erythematosus found an increased risk of candidiasis with high-dose corticosteroids: maximum dose was 24 (range 4-250) and cumulative dose over 3 months was 1.18 g (range 360-4320). These results showed that the risk of candidiasis is related to disease activity, which results in higher systemic steroid requirements. This study aims to evaluate factors associated with the onset of candidiasis in patients with PV at different stages of disease progression.

2. Material and Methods

In this study, the medical records of 100 patients with a diagnosis of pemphigus vulgaris were retrospectively analyzed. The patients were randomly selected from two second-care hospitals over a period of 10 years (between January 2010 and December 2019). The diagnosis of PV was confirmed by clinical, histopathologic, and immunologic criteria in accordance with an international expert panel [6]. Epidemiologic data on demographics, disease characteristics indicating disease activity and severity, comorbidities including diabetes, hypertension, cardiovascular and cerebrovascular disease, indicated treatments (oral steroid dose, adjuvant, and steroid pulse), biochemical parameters, candidiasis history, candidiasis treatment, and PV prognosis or outcome (death) were meticulously recorded.

Patients were categorized into those who developed candidiasis during the follow-up period and those who did not develop candidiasis. All forms of candidiasis, including cutaneous, oral, vaginal, and blood, were recorded.

Potential risk factors for candidiasis, as well as factors associated with pemphigus vulgaris or immunosuppressive therapy that may contribute to the incidence of candidiasis, were documented in the present study. The risk factors included the presence of sepsis, immunosuppressive factors, and the use of corticosteroids or other immunosuppressant. Biochemistry and serology markers associated with systemic inflammation were also calculated.

As this was a retrospective study with no patient data and no intervention, ethics committee approval was not necessary, and only the study completion was reported.

Statistical analysis

Statistical analysis was performed using SPSS version 24 (IBM NY, USA) for Windows. Descriptive and comparative tests, including chi-squared and Student's t-tests, were performed for categorical and numerical variables, respectively, to compare patients with and without candidiasis, and multivariate regression analysis was performed to determine the association between various study factors and candidiasis development. Statistical significance was defined as a p-value less than 0.05.

3. Results

3.1. Demographic, clinical and treatment characteristics

Patient demographic and clinical data are shown in Table 1. The female to male ratio was 1.6:1 with 62 (62%) female and 38 (38%) male patients included in the study. The mean age of the patients was 47.94 ± 10.42 years (range, 28 to 68 years). The majority of the patients selected were either in the active phase of the disease or in the remission phase.

Table 1. Demographic and clinical characteristics of PV patients.

Patient characteristics	Distribution (n= 100)
Age, years, mean ± SD (Range)	47.94 ± 10.42 (28-68)
Male/Female, n (%)	38 (38) / 62 (62)
Patients who relapsed, n (%)	20 (20)
Patients with active disease *	40 (40)
Patients with remission, n (%)	40 (40)

* Active disease: it was defined as the appearance of more than 5 blisters per week and the Nikolsky or Asboe Hansen sign.

3.2. Candida species distribution

Table 2 presents a list of etiological agents associated with candidiasis in PV patients. Candidiasis in PV is commonly associated with *C. albicans*, although in 32% of the cases (27 patients), it was not possible to isolate the causative agent. Systemic treatment was used in the majority of cases to treat candidiasis due to the immunosuppression by the treatment. The mucosal ulceration caused by PV results in severe pain and makes topical treatment difficult, thus necessitating systemic approaches. The most common systemic treatment used was fluconazole (34%) followed by itraconazole (32%).

Table 2. Candida species and antifungal treatments in PV patients with candidiasis.

Characteristic	Distribution, n= 79 (%)
Candida species (85 isolates in 79 patients)	
C.albicans	40 (47)
C.glabrata	8 (9)
C.tropicalis	4 (5)
C.parapsilosis	4 (5)
C.krusei	2 (2)
Candida sp	27 (32)
Antifungal treatment (n=79)	
Topical antifulgal	20 (25)
Fluconazole	27 (34)
Itraconazole	25 (32)
Voriconazole	7 (9)

3.3. Comparative characteristics in patients with PV with and without candidiasis

Comparative characteristics of patients experiencing PV with and without candidiasis are presented in Table 3. Demographic variables and comorbidities did not significantly differ between the two groups. However, NLR and PLR, two variables associated with systemic inflammation, showed substantial differences between the two groups ($P= .001$ and $P= .002$, respectively). Patients who developed candidiasis received a higher dose of corticosteroids, which is indicative of the greater severity of the disease and the consequent need for high doses of corticosteroids, which are typically administered in megadoses (pulse therapy) (Table 3).

3.4. Underlying comorbidities

Comorbidities were detected in 46% of the PV cases, with 37 patients having one or more candidiasis events. In those without a history of candidiasis, 9 patients had comorbidities, but no significant difference was found. Hypertension, diabetes mellitus, chronic renal insufficiency, and coronary artery disease were the most common comorbidities in both groups. Malignancy was observed in only 10 cases. Table 3 shows the distribution of comorbidities among the patients studied.

Table 3. Comparative characteristics of PV patients with and without candidiasis.

Variables	All patients (n= 100)	Candidiasis Absent (n= 21)	Present (n= 79)	P-value
Age, mean ± SD	47.94 ± 10.42	50.38 ± 10.75	46.17 ± 9.99	NS
Gender, female	62 (62)	14 (67)	50 (63)	NS
Any comorbidity	46 (46)	9 (43)	37 (47)	NS
Diabetes	28 (28)	8 (38)	20 (25)	NS
Hypertension	37 (37)	8 (38)	29 (37)	NS
Coronary artery disease	12 (12)	4 (19)	8 (10)	NS
Chronic renal disease	15 (15)	7 (33)	8 (10)	NS
Malignancy	10 (10)	3 (14)	7 (9)	NS
Cerebrovascular events	5 (5)	1 (5)	4 (5)	NS
NLR, mean ± SD	3.6 ± 2.9	2.68 ± 0.91	4.16 ± 1.14	.001
PLR, mean ± SD	183.23 ± 89.4	155.25 ± 49.7	237.55 ± 63.16	.002
PNR, mean ± SD	60.25 ± 18.35	59.78 ± 12.84	57.38 ± 5.17	NS
Sepsis	24 (24)	5 (24)	19 (24)	NS
Candida spp in oral cavity	36 (36)		36 (45)	
Candida spp in genital mucosae	35 (35)		35 (44)	
Candida spp in skin	29 (29)		29 (37)	
Candida spp in urine sample	15 (15)		15 (19)	
Candidemia	14 (14)		14 (18)	
Prior antibiotic including extended spectrum antibiotic	39 (39)	5 (24)	34 (43)	.015
Prior antifungal agent	27 (27)	3 (14)	24 (30)	.019
Pulse corticosteroid therapy	46 (46)	3 (14)	43 (54)	.001
Maximum dose of corticosteroid (mg/day)	55.32 ± 18.49	51.9 ± 5.58	67.67 ± 12.09	.012
Latest dose of corticosteroid (mg/day)	15.28 ± 8.33	6.07 ± 2.02	17.83 ± 7.6	.001
3 months cumulative dose of corticosteroid (mg)	3249 ± 1523	2602.1 ± 482.72	3602.17 ± 886.26	.012
Rituximab	30 (30)	6 (28)	24 (30)	NS
Azathioprine	88 (88)	18 (86)	70 (89)	NS
Mofetil mycofenolate	38 (38)	7 (33)	31 (39)	NS
Overall death	12 (12)	1 (5)	11 (14)	.025

SD= Standard Deviation; NLR= Neutrophil-Lymphocite Ratio; PLR= Platelet-Lymphocite Ratio; PNR= Platelet-Neutrhophil Ratio.

Death rates were significantly higher in patients with candidiasis than in those without candidiasis (14% vs 5%, *P*=.025). This suggests that these patients had increased disease severity, requiring higher doses of corticosteroids and other immunosuppressive agents, particularly azathioprine, resulting in a fatal outcome.

3.5. Identified Risk Factors

Risk factors for candidiasis in patients with PV were determined through a multivariate analysis, as presented in Table 4. Several factors may influence the development and predisposition to candidiasis in patients with PV, including age 65 years or older, female sex, sepsis, disease relapse or activity, use of pulse therapy (high-dose steroids), and elevated NLR ≥2 and PLR ≥150.

Table 4. Multivariate analysis of the risk factors for candidiasis in PV patients.

Variable	OR	95%CI	*P*-value
Age (≥65 years)	**1.5**	**0.92-3.23**	**.038**
Gender (Female)	**1.45**	**1.23-3.38**	**.025**
Comorbidity	0.58	0.26-1.38	.078
Diabetes mellitus	0.78	0.4-1.86	.123
Hypertension	0.85	0.71-1.89	.14
Coronary artery disease	0.45	0.28-1.39	.33
Chronic renal disease	0.38	0.27-2.22	.146
Malignancy	1.28	0.42-3.84	.066
Cerebrovascular event	1.65	0.19-4.58	.079
Sepsis	**2.78**	**1.25-7.36**	**.025**
PV Relapse	**3.25**	**1.89-7.23**	**.015**
Active PV	**2.89**	**1.15-4.35**	**.028**
Maximum corticosteroid dose (≥50mg/day)	**4.85**	**1.87-6.43**	**.001**
Pulse corticosteroid therapy	**3.59**	**2.23-4.89**	**.002**
Prior antibiotic	**6.48**	**1.12-7.23**	**.042**
Prior antifungal	**3.45**	**1.22-3.33**	**.035**
Mycophenolate mofetil	0.65	0.33-0.98	.04 *
Rituximab	1.1	0.45-1.23	.13
NLR (≥2)	**3.38**	**1.27-4.59**	**.001**
PLR (≥150)	**2.85**	**1.84-3.59**	**.001**
PNR (≥50)	1.12	0.24-2.23	.057

NLR= Neutrophil-Lymphocite Ratio; PLR= Platelet-Lymphocite Ratio; PNR= Platelet-Neutrhophil Ratio; * Protective effect.

3.6. Source of candidiasis

Candida albicans was isolated from the majority of cases (47 percent), and the most common sites were oral (36 percent) and genital (35 percent), as well as skin (29 percent) and urine (15 percent) samples. Candidemia was present in 14 patients, 8 of whom (57 percent) had a history of *Candida* isolations from two or more sites. The genital mucosa (14 cases) and urine (8 cases) were the most common sites of isolation in patients with candidemia. *Candida glabrata* was the most common non-albicans species isolated from the genital mucosal and urinary tracts in patients with candidemia, with four and three cases, respectively. None of the specimens were tested for sensitivity.

3.7. Mortality in pemphigus vulgaris with candidiasis

A total of 12 fatal cases were observed in this study, 11 of which occurred in patients with a history of candidiasis. Candidemia was present in 5 of these cases (45%), with C. albicans as the sole cause of isolation. *C. albicans* (8 cases), *C. glabrata* (3 cases), *C. parapsilosis* (3 cases), and *C. tropicalis* (2 cases) were the causative agents of candidiasis and candidemia in these patients.

All cases of candidiasis in the patients with pemphigus vulgaris who died were treated with intravenous fluconazole. Voriconazole followed by fluconazole was used in only 2 cases.

4. Discussion

This study adds to our knowledge of the prevalence of candidiasis in patients with PV. In addition, it provides new data on the risk factors that influence the presence of candidiasis and candidemia in this patient population.

The incidence of candidiasis and candidemia could be modified according to the characteristics of each hospital and patient group. However, it is possible that patients with PV are at high risk of developing candidiasis and subsequent candidemia due to the numerous risk factors they present.

Currently, in patients with risk factors for candidemia, some treatment guidelines suggest the initiation of empiric therapy. However, it is common for patients with PV to have other factors that may influence the risk of candidemia, such as other immunosuppressive therapies, comorbid conditions, sepsis, and empiric use of broad-spectrum antibiotics, malignancy, intravenous catheterization, urinary catheterization, and intensive care unit admission.

In addition to providing new data on the risk factors that influence the presence of candidiasis and candidemia in this patient population, this study adds to our knowledge of the prevalence of candidiasis in patients with PV.

The incidence of candidiasis and candidemia could be modified according to the characteristics of each hospital and patient group; however, it is possible that patients with PV are at high risk of developing candidiasis and subsequent candidemia due to the numerous risk factors they present.

More than 40 species have been identified as responsible for human candidiasis [9]. Of these, at least 17 are capable of causing invasive disease.[10] However, some are more likely to cause superficial infections than invasive disease.[11] The most common species were *Candida albicans*, *Candida glabrata*, *Candida tropicalis*, *Candida parapsilosis*, and *Candida krusei*, with *Candida albicans* causing 81.3% of cases [12]. Our study shows that this pathogen caused only 47% of cases, which is lower than that reported in the literature. In 32% of cases, it was not possible to isolate the yeast, resulting in unidentified species. Therefore, it can be assumed that the proportion of *C. albicans* is higher in this group, similar to previous research. In another study, it was found that 57.14% of immunocompromised individuals had isolation of *C. albicans*, a prevalence closer to that observed in the present study [13]. *C. (Nakaseomyces) glabrata* was the second most common etiologic agent, representing 9% of cases, particularly in women aged 65 years and older, in agreement with existing literature indicating that *C. glabrata* occurs in older women with hematologic malignancies [14]. Unfortunately, molecular techniques to differentiate *Nakaseomyces* species from closely related species *Candida nivariensis* and *Candida bracarensis*, which share similar niches in humans, were not used due to the retrospective nature of the study [15]. The prevalence of *C. albicans* and non-albicans species in PV patients are high.

The median age of the patients participating in the study was 47 years, which is within the range reported in the literature [16]. A female predominance was observed in this study, as in previous epidemiologic studies of PV [17].

Several risk factors have been identified for both candidiasis and candidemia, including the use of broad-spectrum antibiotics in addition to topical and systemic antifungals, which can alter and damage the microbiota, promoting *Candida* colonization [18,19].

In immunocompromised patients and those receiving immunosuppressive therapies, candidiasis is a common complication [20]. And also, it is a common complication among individuals with PV, a rare autoimmune disease of unclear etiology. This is due to the increased need for corticosteroids and other immunosuppressive therapies to manage disease activity, and the increased susceptibility to infection due to skin damage and the development of severe comorbidities that further compromise the immune system [21,22].

A recent study of 25 PV patients showed that 20% of patients had oral candidiasis. C. albicans was predominant in 22/25 isolates, with 100% susceptible to amphotericin and econazole, and 96% susceptible to fluconazole and posaconazole. [23] In our study, antifungal susceptibility testing was not carried out, as it is not a routine test in either of the two hospitals from which the patients were collected. However, all cases were reported to have responded satisfactorily to the treatments given or failed to progress to more severe clinical conditions, except in the cases that develop candidemia.

In previous studies, *Candida* species have been found to be sufficiently susceptible to treatments such as caspofungin, amphotericin, flucytocin, voriconazole and micafungin. Many of these treatments are not available in the hospitals where the study was conducted. Candidiasis with or without candidemia is usually initiated with fluconazole, although resistance rates of between 6 and 25% and even higher have been reported in the literature for nonalbicans species, most notably *C. glabrata* and *C. krusei*, requiring even higher doses of systemic antifungals than in cases associated with *C. albicans*. Other antifungal regimens, such as echinocandins, are recommended for candidemia caused by nonalbicans species [18].

Although topical steroids are not the primary treatment for PV, they are often used to control lesion severity and to reduce the need for systemic steroids, which may contribute to the occurrence of opportunistic infections such as candidiasis. In a study conducted by Lozada et al, which included 55 patients with oral vesicular erosive disease, the effect of adding clobetasol propionate to fluocinolone was observed and 13 patients (24%) were found to have candidiasis at the end of treatment (28 days). [24]

Although there was no difference in the use of mycophenolate mofetil in patients with PV who developed candidiasis compared to those who did not develop candidiasis, it is interesting to note that in the multivariate analysis, mycophenolate use exerted a protective effect against developing candidiasis. Mycophenolate mofetil is an immunosuppressive agent that is used in the avoidance of transplant rejection and in the treatment of autoimmune diseases such as PV. Mycophenolate is a 2-morpholinoethyl ester of mycophenolic acid, the latter being the active form of the mycophenolate mofetil [25].

C. albicans has been shown to be sensitive to mycophenolate when cultured *in vitro* and to inhibit IMP dehydrogenase, the therapeutic target of mycophenolate mofetil [25]. However, previous studies have observed resistance of *C. albicans* to mycophenolic acid, which probably did not allow to observe clear differences between groups and to significantly reduce the risk of infection [26].

Thirty patients were treated using rituximab and no differences between the two groups were observed. Rituximab is a chimeric murine and human monoclonal antibody that selectively targets CD20-positive B-lymphocytes, causing complement-mediated B-lymphocyte lysis, cell cytotoxicity, and induction of apoptosis. It is an effective treatment for PV, but it can cause opportunistic infections, not requiring treatment interruption, but rather infection management [27], and it does not significantly increase the risk of candidiasis as observed in the study.

Rather than being a consequence of immunosuppression associated with systemic steroids, it is likely that the increased incidence of *Candida* plays a greater role in the development of autoimmunity in PV. Superantigens have been shown to induce polyclonal activation of memory T-cells (CD45RO+), resulting in a dysregulated response that may lead to opportunistic infections, primarily *Candida*, and this increased response may be the cause of autoimmune activity in PV [28].

In this study, we found that 79 out of 100 patients with PV at different stages of severity and activity developed candidiasis at some point during the disease, but the underlying factor causing this predisposition has not been elucidated, as it is uncertain whether it is due to the use of immunosuppressive drugs or to other factors.

Corticosteroids are the mainstay of treatment in PV. Such therapies are aimed at suppressing disease activity, inevitably depleting T cells by inhibiting cytokine transcription. In this study, we analyzed several variables related to the steroid requirements for the control of PV activity, such as the maximum steroid dose, the cumulative dose, and the requirements for megadoses of steroids (pulsed therapy), which cause suppression of immune function. Suggested mechanisms to explain the effect of steroids on the development of candidiasis include the reduction of T cells, which affects the immunosuppression that promotes candidiasis, such as occurs in patients with HIV infection, as well as the inhibition of other immune system cells such as macrophages and B cells [29].

In addition, age and gender were associated with a higher risk of candidiasis during the course of the disease, regardless of the use of steroids, but not for comorbid conditions such as diabetes and hypertension.

In addition, we found that the development of candidiasis may be independently influenced by the activity and relapse of PV, as well as the onset of sepsis. Damaged skin in PV may facilitate bacterial and fungal invasion, increasing the risk of infection, which is exacerbated by the increased need for corticosteroids, often administered via pulse therapy, to induce immunosuppression. These factors collectively contribute to increased infection frequency and severity.

Candidiasis is strongly associated with immunosuppressed patients, and in this study we observed that patients with a higher need for immunosuppressant therapy with systemic steroids had a higher incidence of candidiasis. Consequently, the changes observed in markers of systemic inflammation, such as NLR, correlated not only with PV activity, but also with predisposition to candidiasis and candidemia [30].

Two markers of systemic inflammation, NLR and PLR, which are correlated with the activity and severity of PV, were found to be elevated in patients with candidiasis, and elevated levels of these markers were associated with a high risk of developing candidiasis [16]. The elevated levels of NLR presented in this study may be attributed to an activated immune response to PV activity or relapse, as well as bacterial infection resulting in increased neutrophils and decreased lymphocytes, the latter being further more decreased in inflammatory conditions and with megadoses of corticosteroids [16,31].

Additionally, PLR has been proposed as another marker of systemic inflammation, although less studied than NLR [32]. Platelets play a critical role in the inflammatory and tissue repair processes, as supported by a growing body of evidence [33]. Platelets closely contribute with all types of leukocytes, releasing chemotactic substances that expedite leukocyte adhesion to the endothelial surface and their subsequent extravasation [33]. These substances may also have both stimulatory and inhibitory effects on leukocyte inflammatory responses [34]. Chronic low-grade inflammation may increase the PLR and the risk of coronary heart disease, solid tumors and autoimmunity associated with it. Elevated levels of inflammatory markers may contribute to a pro-inflammatory environment that is conducive to the growth of bacterial and fungal infections [35,36].

Several studies have described an increase in the NLR in diverse inflammatory diseases, along with an association between its levels and disease activity, suggesting a prognostic role [37–39]. This increase in NLR results from a rise in neutrophil numbers in the early stages of acute inflammation while lymphocyte numbers are relatively low. At later stages, there is subsequent activation and lymphocyte proliferation in response to chronic inflammation, whereas the number of lymphocytes is relatively low. [40]

We have observed that elevated levels of NLR and PLR may increase the likelihood of acquiring candidiasis and candidemia, possibly due to an increased severity of the disease and a greater need for immunosuppressive drugs, in particular high doses of corticosteroids.

The major strength of our research is that the selection of participants was entirely random from the entire pool of patients with PV from two hospital centers over a considerable period of time, allowing us to avoid selection bias. In addition, because all patients with PV received identical oral treatment and follow-up protocols over time, the patient cohort in this study was likely homogeneous.

However, a major limitation of our study is in its retrospective design, which, in view of the low prevalence of the disease, is an obstacle to the conduct of prospective studies. However, we believe that the patient sample is significant and has sufficient power to draw valid conclusions. To reduce potential selection bias in single-center retrospective studies, patients from two second-care hospitals were randomly selected. To confirm our findings, these results may be complemented by future multicenter studies.

5. Conclusions

Candidiasis in autoimmune patients undergoing immunosuppressive therapy has been linked to a number of risk factors, each of which is controversial in its own right. Finally, immunology studies report that T lymphocyte depression directly influences the development of candidiasis,

although as observed in the results of our study, there are other factors that may contribute to the development of infection in varying degrees.

Clinicians should be aware that the risk of candidiasis in patients with PV may be increased by factors other than corticosteroid use. Monitoring the maximum corticosteroid dose and other serological markers in susceptible patients may help to prevent candidiasis. Patients should also be informed about the risk of candidiasis due to the use of corticosteroids or other factors unrelated to the immunosuppressive effects of the therapies.

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