# КЛІНІЧНА ПРАКТИКА

**UDC 616.517-039:616.5-002.33]-07**
**DOI https://doi.org/10.32782/2226-2008-2025-4-3**

***M. E. Zapolskiy[1] https://orcid.org/0000-0001-9284-3539***
***T. V. Chaban[1] https://orcid.org/0000-0001-6989-5816***
***I. V. Svystunov[2] https://orcid.org/0000-0002-3916-354X***
***L. M. Tymofieieva[1] https://orcid.org/0000-0002-8708-9460***
***D. M. Zapolska[1] https://orcid.org/0000-0002-5721-6836***

## CLINICAL AND DIAGNOSTIC FEATURES OF GENERALIZED FORMS OF PUSTULAR PSORIASIS

[1]Odesa National Medical University, Odesa, Ukraine
[2]Shupyk National Healthcare University of Ukraine, Kyiv, Ukraine

**UDC 616.517-039:616.5-002.33]-07**

**M. E. Zapolskiy[1], T. V. Chaban[1], I. V. Svystunov[2], L. M. Tymofieieva[1], D. M. Zapolska[1]**
**CLINICAL AND DIAGNOSTIC FEATURES OF GENERALIZED FORMS OF PUSTULAR PSORIASIS**
*[1]Odesa National Medical University, Odesa, Ukraine*
*[2]Shupyk National Healthcare University of Ukraine, Kyiv, Ukraine*

Generalized pustular psoriasis (GPP, von Zumbusch disease) is a rare auto inflammatory disease that belongs to the neutrophilic dermatoses; the most severe form of psoriatic disease, which threatens the lives of patients and requires intensive therapy from the first hours of the disease. The mortality rate in case of inadequate therapy reaches 2–4%. If plaque forms of psoriasis do not pose diagnostic difficulties, pustular forms of psoriasis are often mistaken for eczema, bullous toxidermia, herpes, Andrews' pustular bacterioides, subcorneal pustulosis, etc.

The research **aims** to study the clinical features course of various forms of pustular psoriasis in patients depending on the provoking factors.

**Materials and methods.** Under our observation for 5 years, there were 57 patients with pustular psoriasis (with limited forms of pustular psoriasis – 34, with widespread – 23), who were treated at the Department of Dermatology and Venereology of Odesa Regional Clinical Hospital and at the multidisciplinary medical center "Renaissance Medical". The diagnosis of pustular forms of psoriasis was established on the basis of anamnesis data, clinical manifestations of the disease, laboratory tests, using the ICD-10 classification.

**Results.** Analysis of 57 cases of pustular forms of psoriasis: limited, widespread, generalized (von Zumbusch disease), juvenile pustular psoriasis, Acrodermatitis continua of Hallopeau, Barber's palmoplantar pustulosis allowed us to identify a set of clinical and diagnostic criteria and distinguish GPP, from dermatoses that mimic it, make a timely diagnosis, and prescribe adequate therapy. This is especially important considering that morphological changes in GPP, dermatoscopic signs do not have sufficient specifics and cannot be used in differential diagnostic screening.

**Keywords:** generalized pustular psoriasis, clinical and diagnostic criteria.

**УДК 616.517-039:616.5-002.33]-07**

**М. Е. Запольський[1], Т. В. Чабан[1], І. В. Свистунов[2], Л. М. Тимофєєва[1], Д. М. Запольська[1]**
**КЛІНІКО-ДІАГНОСТИЧНІ ОСОБЛИВОСТІ ГЕНЕРАЛІЗОВАНИХ ФОРМ ПУСТУЛЬОЗНОГО ПСОРІАЗУ**
[1]Одеський національний медичний університет, Одеса, Україна
[2]Національний університет охорони здоров'я України імені П. Л. Шупика, Київ, Україна

Генералізований пустульозний псоріаз (ГПП) – рідкісне аутозапальне захворювання, яке належить до нейтрофільних дерматозів; найважча форма псоріатичної хвороби, що загрожує життю пацієнтів і потребує інтенсивної терапії вже з перших годин захворювання. Пустульозні форми псоріазу нерідко приймаються за екзему, бульознутоксикодермію, герпес, бактерід пустульозний Ендрюса, пустульоз субкорнеальний тощо. Стаття присвячена особливостям клінічного перебігу різних форм пустульозного псоріазу. Аналіз 57 випадків пустульозного псоріазу у хворих, що проходили лікування в шкірно-венерологічному відділенні КНП ОРКПЦ ООР м. Одеси та в багатопрофільному медичному центрі Ренесанс Медікал з 2018 по 2023 рр., дозволив визначити низку клініко-діагностичних критеріїв генералізованого пустульозного псоріазу, що дозволяють відокремити ГПП від дерматозів, що його імітують, своєчасно поставити діагноз і призначити раціональну терапію.

**Ключові слова:** генералізований пустульозний псоріаз, клініко-діагностичні критерії.

## Introduction

Generalized pustular psoriasis (GPP, von Zumbusch disease), in the English-language literature – generalized pustular psoriasis is a rare autoinflammatory disease that belongs to the neutrophilic dermatoses, characterized by the formation of widespread sterile pustules, erythema, and deterioration of the patient's general condition. GPP is associated with an increased risk of mortality and disability. Unlike plaque forms of the disease, characterized by deregulation of adaptive immunity, pustular psoriasis is associated with dysfunction of innate immunity and contributes to the persistent activation of autoinflammatory processes in the human body [6; 8].

Pustular psoriasis can occur as a result of the transformation of already existing plaque forms of the disease or primarily, in completely healthy individuals. In the practice of a dermatologist, generalized pustular psoriasis occurs much less frequently than plaque forms and accounts for approximately 2% of cases of the total number of patients with psoriasis. GPP is considered one of the most severe forms of psoriatic disease, which threatens the life of patients. In contrast to localized forms of pustular psoriasis (Barber's palmoplantar pustulosis, limited pustular psoriasis), generalized forms are considered an emergency in dermatology, requiring intensive therapy from the first hours of the disease. The mortality rate in case of inadequate therapy of von Zumbusch disease reaches 2–4% [3; 4].

Scientists have drawn attention to the importance of studying the pathogenesis of individual clinical forms of pustular psoriasis with the subsequent selection of optimal narrowly targeted therapeutic and preventive strategies. A sign of inappropriate activation of the adaptive immune system is increased activity of T- lymphocytes and increased production of a number of pro-inflammatory cytokines, in particular interleukin-17 (IL-17). GPP is considered an autoinflammatory process associated with neutrophilic, non-infectious tissue damage against the background of inhibition of signaling pathways of cytokine expression [3; 9].

Although blocking IL-17 provides a moderate therapeutic effect in GPP, the main reason for the violation of neutrophil chemotaxis processes is linked with a high concentration of IL-36 in peripheral tissues, which is responsible for innate immunity and accumulates mainly in human skin. The IL-36 cytokine family consists of three agonists with proinflammatory activity (IL-36α, IL-36β, and IL-36γ) and one antagonist with anti-inflammatory effect (IL-36Ra). It has also been shown that the activation of proinflammatory cytokines in pustular psoriasis is regulated by a number of enzymes that originate mainly from keratinocytes, including: cathepsin-G, protease-3, serine protease, elastase. It is believed that keratinocytes provide the main regulatory function in GPP [1; 3].

Further insights into the pathogenesis of generalized pustular psoriasis have been gained through genetic studies. Single-locus mutations have been identified that lead to disruption of a number of immunoregulatory processes in areas of inflammation, the main of which are mutations of the IL1RN complex – the receptor for the antagonist of interleukin-1. Other mutations identified in GPP include missense mutations affecting the activity of the IL-36 receptor antagonist (homozygous missense mutation IL-36RN), caspase recruitment domain-containing protein-14 (CARD14), adaptor protein complex 1 subunit sigma-3 (AP1S3), serine protease inhibitor serpin family 3 (SERPINA3), serine protease inhibitor serpin family 1 (SERPINA1), neutrophil enzyme myeloperoxidase (MPO), and TNFAIP3-interacting protein-1 (TNIP1) [2; 3].

Recent genetic studies suggest that GPP may be considered as one of the variants of a new autoinflammatory condition – DITRA (deficiency of IL-1 receptor antagonist). Interleukin-36 is a member of the IL-1 family, and mutations that result in deficiency of the receptor antagonist of the same name contribute to increased IL-36 levels, increased tissue inflammation, and increased relapse rates. These findings are supported by the successful use of tocalizumab in autoinflammatory processes, including GPP [4; 5].

The identified genetic mutations explain some differences in the pathogenesis of GPP occurring against the background of plaque psoriasis and without it. The autoinflammatory state of the DITRA type is more characteristic of patients with plaque psoriasis in the anamnesis, and in cases of newly occurring forms of GPP, the autoinflammatory process with an immunoallergic component dominates.

Plaque forms of psoriasis do not pose diagnostic difficulties, especially when it comes to a burdened family history. However, pustular forms of psoriasis (limited, widespread, generalized, Acrodermatitis continua of Hallopeau, Barber's palmoplantar pustulosis), according to the literature, are often confused with eczema, bullous toxicoderma, herpes, Andrews' pustular bacterid, subcorneal pustulosis, etc. [1; 8].

The research **aims** to investigate the features of the clinical course of various forms of pustular psoriasis in patients depending on the provoking factors.

## Materials and methods

Under our observation for 5 years, there were 57 patients with pustular psoriasis (with limited forms of pustular psoriasis – 34, with widespread – 23), who were treated in the dermatovenereological department of the Municipal institution "Dermatology department of the Odessa Regional Oncology Center" and in the multidisciplinary medical center Renaissance Medical. All stages of the study were carried out in compliance with the principles of the Code of Ethics of the World Medical Association (Declaration of Helsinki); patients who participated in the study provided informed consent to the processing of their personal data (study protocol No. 10 dated 01/29/2024).

The diagnosis of pustular forms of psoriasis was established on the basis of anamnesis data, clinical manifestations of the disease, and laboratory tests, using the ICD-10 classification, according to which the following forms of the disease were distinguished:

**L40.1 pustular psoriasis**

(presence or absence of metabolic disorders)

limited form

– common form

– generalized (von Zumbusch disease) form

– herpetiform impetigo (pustular psoriasis of pregnant women)

**L40.1.1 juvenile pustular psoriasis**
limited form
– annular form
– generalized form
**L40.2 persistent acrodermatitis** [Acrodermatitis continua of Hallopeau]
**L40.3.1 palmar and plantar pustulosis**
Barber disease.

**Study results.** Given the rarity of GPP, the study included a limited number of patients with this pathology – 11 people (5 men and 6 women), of whom 4 (7.1%) were children under 12 years of age (Table 1).

As can be seen from Table 1, limited forms of pustular psoriasis were detected in 9 (15.8%) patients, the average duration of the disease in this group of patients was (4.5 ± 0.5) months. In the observation group, palmoplantar forms of pustular psoriasis dominated, which accounted for 19 (33.3%) cases with an average duration of the disease of 1.2 years. Among the patients was one female child (1.8%) aged 9 years. In all cases, the palmar-plantar form showed a chronic and persistent course. Patients expressed concerns regarding the effectiveness of previous treatments (Figure 1).

Another localized form of pustular psoriasis with a predominant acral (hands, feet) localization is Acrodermatitis continua of Hallopeau. In the observation group, it was detected in 3 patients. In one case, the process preceded the generalized form of pustular psoriasis and had difficulties in diagnosis and selection of treatment methods. Also, the causes of activation of Acrodermatitis continua of Hallopeau were aggressive irritating topical therapy in the areas of the hands and feet.

Limited forms of pustular psoriasis were observed quite often – 9 (15.8%) cases, in which the area of skin lesions did not exceed 3%, and the duration of the disease was 4.5 months. One of the reasons for the formation of pustules was inadequate topical therapy using harsh topical agents such as iodine, alcohol-based tinctures, and keratolytics. Pustules often appeared alongside pre-existing psoriatic plaques and were not accompanied by pain or other subjective sensations, as is the case with GPP (Figure 2).

Table 1

**Analysis of the prevalence of pustular forms of psoriasis for the period 2018–2023**

| A form of pustular psoriasis | Total patients | Men | Women | The average duration of the disease |
|---|---|---|---|---|
| Limited (lesions up to 2% of skin area) | 9 (1.6%) | 3 (5.3%) (of which 1 child) | 5 (8.8%) | (4.5 ± 0.5) months |
| Common (damage to 75% of the skin area) | 12 (21.1%) | 5 (8.8%) | 7 (12.3%) | (8.2 ± 0.7) months |
| Generalized pustular psoriasis (lesions more than 75% of the skin area) | 11 (19.3%) | 5(8.8%) | 6 (10.5%) (of which 1 child) | (6.3 ± 0.4) months |
| Annular | 3 (5.3%) | 1 (1.8%) (of which 1 child) | 2 (3.5%) | (3.7 ± 0.8) months |
| Pustular psoriasis of pregnant women | – | – | – | – |
| Palmar-plantar form | 19 (33.3%) | 7 (12.3%) | 12 (21.1%) (of which 1 child) | (1.2 ± 0.5) years |
| Acrodermatitis continua of Hallopeau | 3 (5.3%) | 3 (5.3%) | – | (8.7 ± 1.1) years |
| Total number of patients | 57 (100%) | 25 (43.8%) | 32(66.2%) | (1.9 ± 0.6) years |

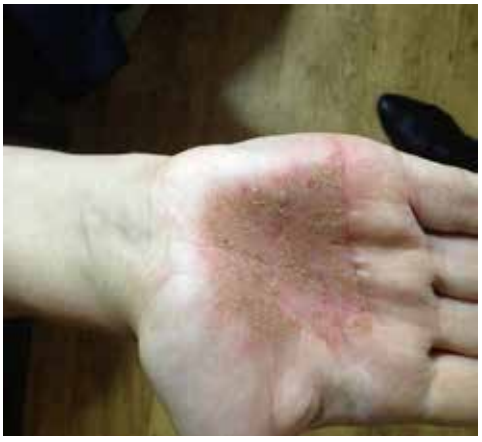


**Fig. 1. Barber's palmoplantar pustulosis**

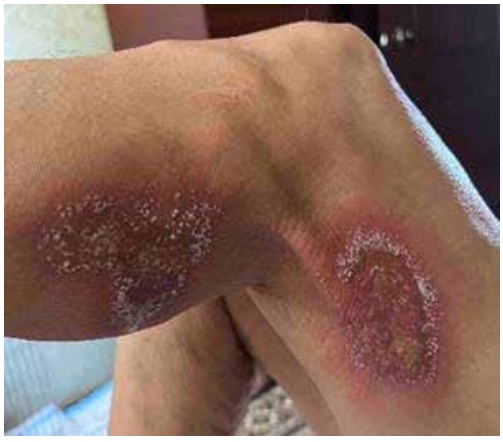


**Fig. 2. Pustular psoriasis, limited form**

Von Zumbusch-type generalized pustular psoriasis was diagnosed in 11 patients (6 women and 5 men). Of the total number of patients, two were children aged 9 and 11 years, in both cases psoriasis appeared for the first time after a respiratory viral infection. GPP in all patients had a severe course: it was accompanied by general toxic symptoms, hypoalbuminemia, hypocalcemia, increased C-reactive protein, persistent leukocytosis. A characteristic feature, in addition to multiple pustules, was persistent erythema of a congestive nature, which persisted for a long time in most patients and after treatment. Timely initiation of biologic therapy prevented the development of post-inflammatory erythema, and was also insignificant in children (Figures 3–6).

Another clinical form affecting extensive skin areas was annular pustular psoriasis (APP), which was generally less severe and more easily managed compared to GPP and usually had a subacute course. Among our patients, APP was detected in 3 people (2 – adults, 1 – child). The clinical feature of this form of psoriasis is the peripheral growth of the lesion, thus the pustules are formed in the form of a circle (Figure 7).

Juvenile pustular psoriasis (JPP) affects children under 12 years of age, and was detected in 2 patients in the observation group. Like von Zumbusch disease, JPP has a severe course with deterioration of the general condition of patients, fever, intense pain in the affected areas, and arthralgia (Figure 8).

No cases of pustular psoriasis in pregnant women were recorded during the study period.

## Discussion

The anamnesis data and clinical manifestations of pustular forms of psoriasis remain quite informative diagnostic criteria. Morphological signs of generalized pustular psoriasis do not have sufficient specificity and are

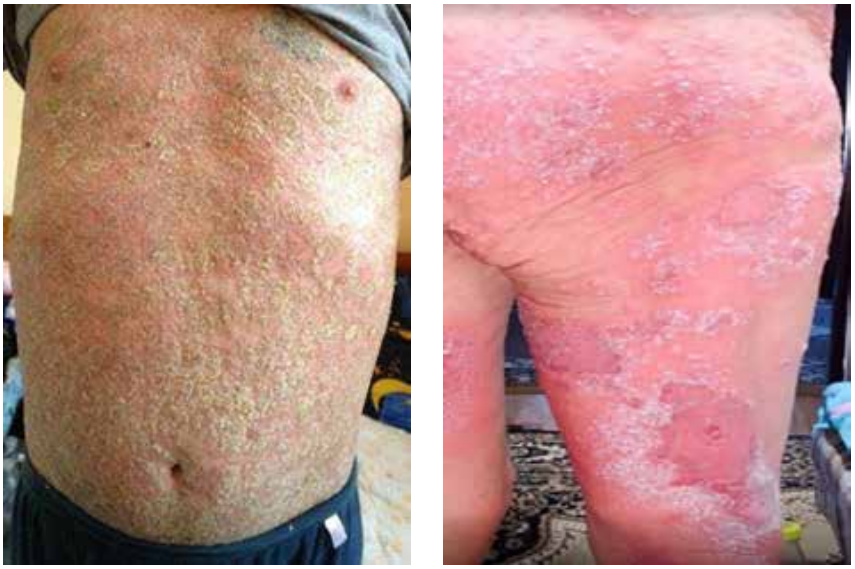
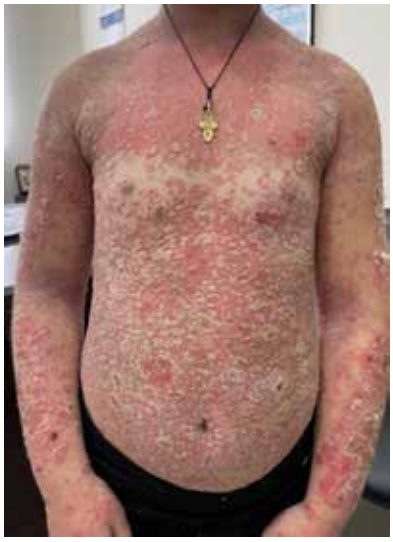


**Fig. 3–4. Generalized pustular psoriasis**



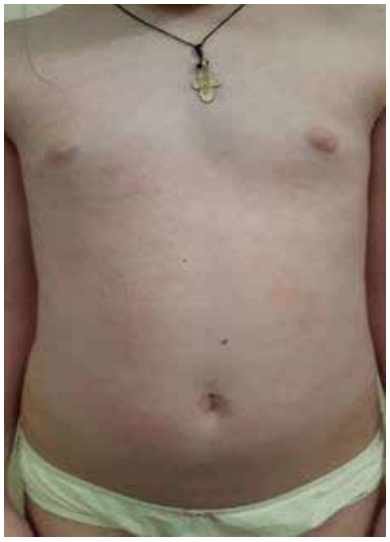


**Fig. 5–6. GPP in a 9-year-old child (use of biological therapy – IL17 inhibitors)**

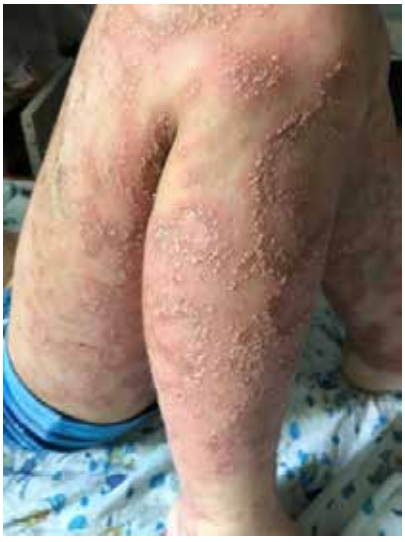


**Fig. 7. Annular pustular psoriasis (a 10-year-old child)**

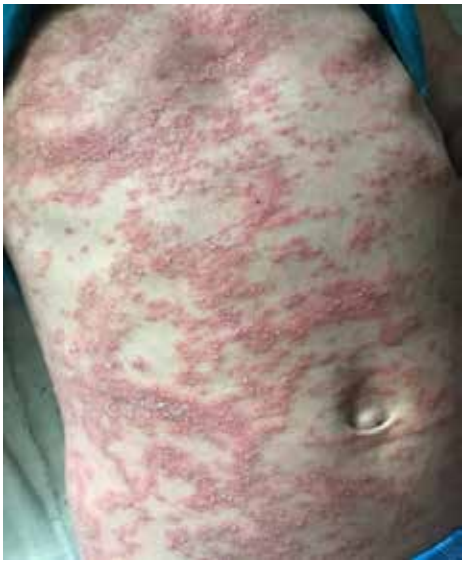


**Fig. 8. Juvenile pustular psoriasis**

similar in many neutrophilic dermatoses. Parakeratosis, epidermal hyperplasia, loss of the granular layer, and pronounced neutrophilic infiltration are typical. The similarity of morphological changes in most neutrophilic and pustular dermatoses does not allow histological research methods to be considered reference in the diagnosis of pustular psoriasis. Additional immunohistochemical studies are important, which takes time.

Dermatoscopic signs characteristic of plaque psoriasis in the form of teardrop-shaped vessels during the transformation of the disease into a pustular form disappear or are less distinct. Already in the early stages of GPP, crater-like elevations, areas of epidermal detachment, and isolated capillary vessels are formed. Dermatoscopy provides limited diagnostic value in GPP.

Generalized forms of pustular psoriasis have a number of clinical features that distinguish it from other pustular dermatoses and help in conducting differential diagnostic screening (Table 2).

A characteristic feature of GPP is the symmetrical distribution of the rash, the appearance of vesicle-pustules in most cases is preceded by soreness, burning of the skin. From the first days of the disease, general toxic symptoms appear. In patients who previously had plaque psoriasis, before the development of GPP, the color of psoriatic papules changes to red or stagnant-cyanotic, most elements acquire an exudative character, the formation of crusts decreases. Increased skin infiltration in such cases helps to suspect plaque psoriasis in the anamnesis.

Unlike acute generalized exanthematous pustulosis and toxic epidermal necrolysis, GPP is much less often associated with the use of medications and is more often associated with acute bacterial-viral infections. However, as can be seen from Table 2, medications can sometimes provoke GPP. Among the main drugs that provoke pustular forms of psoriasis, systemic corticosteroids, beta-blockers, antibiotics, and cold medications are distinguished.

In our observation group, in 5 (8.8%) patients, the use of drugs led to the development of pustular psoriasis.

When diagnosing GPP, special attention should be paid to the localization of pustules, the size and depth of their occurrence, the distance between the elements, the duration of the existence of vesiculopustules, the color of the skin in the affected areas, the presence of fresh pustular elements in the same areas, the nature of the exfoliation of the epidermis on the palms and feet. A characteristic morphological feature of pustular psoriasis is the neutrophilic content of the pustules.

An important clinical feature of GPP is the nature of the course of the disease itself: the process has a tendency to multiple recurrences in the same places, while, unlike

Table 2

**Analysis of diagnostic criteria for generalized pustular psoriasis and other pustular dermatoses**

| Signs | GPP | Subcorneal pustulosis | Bullous toxidermia | Acute generalized exanthematous pustulosis | Toxic epidermal necrolysis |
|---|---|---|---|---|---|
| Acute onset of the disease | +++ | + | ++ | +++ | +++ |
| History of psoriasis | +++ | + | – | – | – |
| Pain in the joints | +++ | + | ++ | +++ | ++ |
| An increase in body temperature to 38°C or higher | +++ | + | ++ | + | ++ |
| Soreness in the affected areas | +++ | + | – | + | ++ |
| Peeling of the epidermis of the palms, soles | – | – | + | + | +++ |
| Respiratory viral infections | +++ | ++ | – | + | + |
| Damage to the nail plates | ++ | – | – | + | ++ |
| Connection with the use of medicines | ++ | + | +++ | +++ | +++ |
| Clustered pustules with neutrophil content | +++ | ++ | – | – | – |

Notes:

"–" is not typical

"+" is rare

"++" occurs with moderate frequency

"+++" occurs with high frequency

subcorneal pustulosis, the skin color in the affected areas changes and acquires a red-blue hue.

It should be noted that pustular forms of psoriasis in children occurred much less frequently than in adults, which is probably due to the high activity of the adaptive mechanisms of the immune system of children. In our observation group, there were only 4 (7%) children with pustular forms of psoriasis, in all cases, thanks to the use of biological therapy (IL-17 inhibitors) and systemic retinoids, a relatively rapid positive effect was achieved.

In the presented study, pustular forms of psoriasis were more common in women, with a total of 32 (56.1%) cases, while in men – 25 (43.9%) cases. Age and gender characteristics of GPP require further study of the influence of the immune and endocrine systems on the course of dermatosis, and studies related to the role of inflammasomes, IL-1ά, IL-36ά in maintaining immunoinflammatory processes in pustular forms of psoriasis deserve special attention [3; 7].

Thus, a dermatovenerologist must timely and correctly analyze the history of the disease, previous interventions, heredity, and most importantly, separate GPP from dermatoses that mimic it, such as subcorneal pustulosis, bullous disseminated streptoderma, generalized impetigo (acute generalized exanthematous pustulosis).

## Conclusions

1. Among the main trigger factors of generalized pustular psoriasis, the following should be distinguished: stress, medications (systemic corticosteroids, beta-blockers, antibiotics), and respiratory viral infections.

2. A characteristic feature of generalized pustular psoriasis is a stable, wave-like course with a tendency to re-form pustules in the same areas.

3. Generalized pustular psoriasis in our cohort was in the second place in terms of frequency of detection. The most common manifestation of pustular psoriasis was the palmar-plantar form of dermatosis, detected in 19 (33.3%) individuals.

4. Age and gender characteristics of von Zumbusch disease and the influence of the immune and endocrine systems on the course of dermatosis require further study.

## BIBLIOGRAPHY


1. Fujita H, Gooderham M, Romiti R. Diagnosis of generalized pustular psoriasis. *Am J Clin Dermatol*. 2022; 23(Suppl 1): 31–38. doi: 10.1007/s40257-021-00652-1.
2. Gooderham MJ, Van Voorhees AS, Lebwohl MG. An update on generalized pustular psoriasis. *Expert Rev Clin Immunol*. 2019; 15(9): 907–919. doi: 10.1080/1744666X.2019.1648209.
3. Goyal PK, Mohammed TO, Mahmoud A, Zaidi AJ, Nguyen CV. COVID-19 infection leading to acute pustular dermatoses. *Arch Dermatol Res*. Published Online November 1. 2022; 1–13. doi: 10.1007/s00403-022-02450-z.
4. Hoegler KM, John AM, Handler MZ, Schwartz RA. Generalized pustular psoriasis: a review and update on treatment. *J EurAcad Dermatol Venereol*. 2018; 32(10): 1645–1651. doi: 10.1111/jdv.14949.
5. Kara Polat A, Alpsoy E, Kalkan G, et al. Sociodemographic, clinical, laboratory, treatment and prognostic characteristics of 156 generalized pustular psoriasis patients in Turkey: a multicentre case series. *J EurAcad Dermatol Venereol*. 2022; 36(8): 1256–1265. doi: 10.1111/jdv.18103
6. Ly K, Beck KM, Smith MP, Thibodeaux Q, Bhutani T. Diagnosis and screening of patients with generalized pustular psoriasis. *Psoriasis (Auckl)*. 2019; 9: 37–42. Published 2019 Jun 20. doi: 10.2147/PTT.S181808.
7. Mahil SK, Catapano M, Di Meglio P, et al. An analysis of IL-36 signature genes and individuals with IL1RL2 knockout mutations validates IL-36 as a psoriasis therapeutic target [published correction appears in Sci Transl Med. 2017 Dec 13;9(420)]. *Sci Transl Med*. 2017; 9(411): eaan2514. doi: 10.1126/scitranslmed.aan2514.
8. Prinz JC, Choon SE, Griffiths EM, et al. Prevalence, comorbidities and mortality of generalized pustular psoriasis: A literature review. *J EurAcad Dermatol Venereol*. 2023; 37(2): 256–273. doi: 10.1111/jdv.18720.
9. Zhou J, Luo Q, Cheng Y, Wen X, Liu J. An update on genetic basis of generalized pustular psoriasis (review). *Int J Mol Med*. 2021; 47(6): 118. doi: 10.3892/ijmm.2021.4951.


*Надійшла до редакції 07.02.2025 р.*
*Прийнята до друку 01.09.2025 р.*
*Електронна адреса для листування maksym.zapolskyi@onmedu.edu.ua*