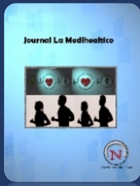

JOURNAL LA MEDIHEALTICO

VOL. 05 ISSUE 04 (890-897), 2024
DOI: 10.37899/journallamedihealtico.v5i4.1584

Profile of Generalized Pustular Psoriasis Inpatient Installation at Dr. Moewardi General Hospital Surakarta from January 2018-December 2022

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Article Info

Article history:
Received 11 August 2024
Received in revised form 7 September 2024
Accepted 30 September 2024

Keywords:
Psoriasis
Pustular Psoriasis
Immunosuppressant
Corticosteroid

Abstract

Generalized pustular psoriasis (GPP) is a form of psoriasis characterised by the presence of sterile pustules. Its prevalence is between 2 and 3.5% of the population worldwide and in Indonesia it is 2.5% of the population. It can cause severe physical and psychosocial distress affecting the patient's quality of life. Objective: To describe the profile of GPP patients treated in the inpatient installation of Dr. Moewardi Hospital, Surakarta in the period of January 2018-December 2022. A retrospective descriptive study was conducted using the secondary data of medical records of GPP patients treated in the inpatient installation of Dr. Moewardi Hospital from January 2018 to December 2022. Results: In the 5-year period, there were 23 GPP inpatients, predominated by female (78.26%) with the age ranged from 5 to 74 years old. Generalised pustular psoriasis mostly affected the age group of 41- 50 years old (26.04%). Most patients were hospitalized for 6–10 days (39.13%). The most common therapy was immunosuppressant (65.2%) followed by oral corticosteroids (26.1%) and zinc (17.4%). Most patients also received moisturizer therapy (56.5%). Generalised pustular psoriasis mostly affects people aged between 41 and 50 years old. Females are more prone to GPP. The therapy given are oral immunosuppressive regimens, oral corticosteroids, zinc, topical corticosteroids and moisturizers.

Introduction

Generalized pustular psoriasis (PPG) is a form of psoriasis characterized by the presence of sterile pustules. Pustules can be widespread or localized and are characterized by the presence of sterile neutrophilic infiltration. Psoriasis is a chronic cellular inflammatory disease that affects the skin, nails and/or joints, often found in two age groups, namely children <18 years old and adults. Psoriasis is estimated to affect 2.0-3.5% of the population worldwide. The prevalence of psoriasis patients reaches 2.5% of the population in Indonesia and from this figure, there are still many who have not received proper medical treatment. Data from several hospitals in Indonesia in 2003-2006 as many as 96 or 0.4% of new cases of psoriasis occurred under the age of 15 years out of a total of 22,070 new patient visits. In general, PPG is more common in women and can appear in all age groups and is more common in adults, namely in the fourth and fifth decades of life. In children, PPG is more common in males than females (3:2) ranging from 0.6% to 7% of cases (Evanti et al., 2022; Ilona & Irawanto, 2018; Kimmel & Lebwohl, 2018; Mirza et al., 2018; Romiti et al., 2022). Generalisata pustular psoriasis initially appears as red papules or plaques that quickly develop into yellowish superficial pustules with an erythematous base and can present with systemic symptoms such as fever,

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joint pain, headache and leukocytosis. PPG can cause severe physical and psychosocial disorders and have a considerable impact on the patient's quality of life (Armstrong & Read, 2020).

The diagnosis of PPG is established based on the clinical morphology and location of the lesion. Histopathology is not very necessary but can help to distinguish psoriasis from other dermatosis diseases. Histopathological examination can show a pattern of psoriasis reaction defined by the presence of epidermal hyperplasia with lengthening (Raharja et al., 2021) of the rete ridge with enlargement of the bulb at the end. The skin papillae contain dilated, dense and sinuous capillaries, and the suprapapillary plates appear very thin. The histopathological picture also has superficial infiltration, perivascular initially dominated by lymphocytic and neutrophilic and parakeratosis is found which is initially focal and then confluent containing a typical collection of neutrophils called Munro microabscesses (Gisondi et al., 2020).

In the last decade, there has been a lot of research on the epidemiology of psoriasis, especially in developing countries. The latest study extracted information from health databases that were collected on a regular basis and were more representative nationally than in previous studies. PPG cases over the past few years have been found quite a lot at Dr. Moewardi Surakarta Hospital, therefore this study was made to update the profile of PPG patients, especially in the inpatient installation of Dr. Moewardi Surakarta Hospital (Parisi et al., 2020). This study aims to determine the profile of PPG patients in the inpatient installation of Dr. Moewardi Surakarta Hospital for the period January 2018 – December 2022.

Methods

This study is a retrospective descriptive research using secondary data from the patient's medical records taken from the medical records of the inpatient installation of Dr. Moewardi Surakarta Hospital in the period January 2018 – December 2022. The inclusion criteria in this study are patients with a diagnosis of PPG based on the international classification of diseases (ICD 10) L40 for PPG in the inpatient unit at RSDM for the period January 2018 – December 2022. The exclusion criteria in this study are patients with incomplete data and do not meet the research criteria. The characteristics of this study include prevalence, gender, age, length of treatment and type of therapy. All results of this research are compiled in the form of tables and explained in the form of narratives.

Result and Discussion

Patients with a history of visits to inpatient installations diagnosed with ICD code 10 L40 for PPG in the period January 2018 – December 2022 were 34 people. The data was then adjusted to the research criteria and data duplication was removed so that 23 patients were obtained within the last 5 years who were the subjects of the study. The patient profile is listed in table 1.

Table 1. Characteristics of the research subject

Characteristic	Number (n)	Percentage (%)
Prevalence		
2018	8	34,78
2019	5	21,74
2020	3	13,04
2021	4	17,39
2022	3	13,04
Gender		
Man	5	21,74
Woman	18	78,26
Age		

ISSN 2721-1215 (Print), ISSN 2721-1231 (Online)
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0-10 years	1	4,34
11-20 years	2	8,68
21-30 years old 31-40 years old 41-50 years old 51-60 years old >60 years	3 5 6 1 5	13,02 21,79 26,04 4,34 21,79
Length of Treatment		
0-5 Days	8	34,78
6-10 Days	9	39,13
>10 Days	6	26,09
Types of Therapy		
Immunosuppressants (Cyclosporin/ methotrexate)	15	65,2
Oral Corticosteroids (Methylprednisolone)	6	26,1
Zink	4	17,4
Topical corticosteroids (Betamethasone, desoxymethasone, mometasone)	11	47,8
Moisturizer	13	56,5

PPG patients in inpatient installations in 2018 had 8 patients (34.78%), in 2019 5 patients (21.74%), in 2020 3 patients (13.04%), in 2021 4 patients (17.39%) and in 2022 3 patients (13.04%). The female gender was more than that of men, namely 18 female patients (78.26%) and 5 male patients (21.74%).

The distribution of PPG patients by age group was obtained in the age group of 0-10 years as many as 1 patient (4.34%), the age group of 11-20 years 2 patients (8.68%), the age group of 21-30 years 3 patients (13.02%), the age group of 31-40 years 5 patients (21.79), the age group of 41-50 years 6 patients (26.04%), the age group of 51-60 years 1 patient (4.34%) and the age group of >60 years 5 patients (21.79%).

Most of the patients received immunosuppressant therapy, namely methotrexate or cyclosporine for 15 patients (62.2%), oral corticosteroids for 6 patients (26.1%), zinc given to 4 patients (17.4%), topical corticosteroid treatment such as betamethasone, desoxymethasone and mometasone for 11 patients (47.8%) and *moisturizers* given to 13 patients (56.5%). Patients who were hospitalized for 0-5 days were 8 patients (34.78%), the length of treatment was 6-10 days, 9 patients (39.13%) and the length of treatment > 10 days was 6 patients (26.09%).

Generalisata pustular psoriasis is the most severe variant of psoriasis characterized by the onset of intermittent extensive cutaneous erythema, covered by pustules, systemic symptoms and extra-cutaneous manifestations such as arthritis, uveitis, acute respiratory distress syndrome, cardiovascular shock and cholestasis (Gisondi et al., 2022). PPG is characterized by the presence of several sterile pustules that are fused and can be localized or generalized.

Generalized pustular psoriasis begins with a fever that lasts several days and the onset of a sterile pustule eruption with a diameter of 2 to 3 mm. On the patient's skin, a broad reddish rash will appear, then within a few hours a sterile pustule will appear that spreads and partially fuses. PPG predilection can affect any part of the skin, but it is more common in the torso and upper and lower extremities. Lesions can appear on initially healthy skin or on pre-existing

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plaque psoriasis lesions. Pustular exanthema of the oral mucosa may occur during periods of exacerbation and persistent (Twelves et al., 2019) *geographic tongue* may appear and on the lips may indicate desquamation and ulceration.

Generalized pustular psoriasis is divided into subtypes von Zumbusch, namely a complete pustular eruption and spread with systemic symptoms such as fever and arthralgia. The annular subtype is an annular lesion with pustules along the edges, the exantematic subtype is an acute pustular eruption without systemic symptoms that disappears after a few days and the herpetiformis impetigo subtype is PPG that occurs during pregnancy. PPG (Shah et al., 2019) has 3 phases, namely the pre pustular phase, *the flare phase* and the post flare chronic phase which can continue to the next *flare* phase. This recurring pattern can continue episodically throughout life. The appearance of infections and the use of certain drugs can trigger or worsen the disease.

Psoriasis pustular generalisata is one of the rare skin diseases, inaccurate diagnosis enforcement poses challenges in estimating the prevalence of PPG disease. PPG can affect all populations and its prevalence varies based on geographic area. A study conducted in 2004 by Parisi et al. in France using a questionnaire-based assessment in 121 hospitals showed 99 cases of PPG in 46 different hospitals, so that the prevalence of the disease is estimated to be 1.76 cases per 1,000,000 people. Research by Morita et al. in 2021 also reported the prevalence using a questionnaire sent to 575 community center hospitals throughout Japan and recorded details of PPG patient visits from 1983 – 1989, the study involved 541 patients with PPG and reported an estimated PPG case of 7.46 patients per 1,000,000 people with 2.87 patients per 1,000,000 people experiencing PPG. A review of (Parisi et al., 2020) the national insurance claims database in the Republic of Korea conducted in 201-2015 estimated the prevalence of PPG at 1.2 cases per 10,000 people. Psyen with psoriasis ranged from 219,429–233,909 or as many as 2.0%–2.7% who suffer from PPG, this shows that the prevalence and epidemiological data of PPG vary from year to year. Research conducted by Kristiani et al in 2016 in Indonesia reported that the prevalence of PPG reached 7.46 cases per 1,000,000 people. In this study, 23 PPG patients were found in the last 5 years (Kristiani & Anggraini, 2020).

A study conducted by Choon et al in 2014 reported 102 patients in Malaysia with a PPG ratio of 2:1 in women compared to men. Research conducted by Morita et al. in 2021 on more than 700 PPG patients in Japan found that 51.5% of PPG patients were female. Zheng et al. (2022) found that the increased risk of PPG was due to the involvement of the AP1S3 gene (Adaptor Related Protein Complex 1 Subunit Sigma 3) which contributes to the pathogenesis of GPP. The AP1S3 gene has a mutation so that it loses its function. Zheng et al. found that 95% of individuals who experienced this gene variation were female. PPG can occur at any age, but most cases of PPG appear at the age of 40-50 years. In this study, the dominant age in PGG was obtained at the age of 41-50 years (26.04%), more common in women than men with the number of female patients 18 patients (78.26%) and men 5 patients (21.74%) (Choon et al., 2014; Mirza et al., 2018; Miyachi et al., 2022; Morita et al., 2021; Romiti et al., 2022; Zheng et al., 2022).

The pathogenesis *of flares* in PPG is still unclear, but the pathogenesis of PPG can lead to genetic mechanisms of autoinflammation and autoimmunity. IL36RN mutations have been identified in sporadic and familial cases of PPG worldwide. The presence of functional mutations in the interleukin (IL)-36 receptor antagonist results in hyperactivation of IL-36 signaling due to unimpeded stimulation of IL-36 receptors by its ligands, IL-36α, IL36β and IL-36γ. Increased production of IL-36 induces chemokine production by keratinocytes, leading to an accumulation of epidermal neutrophils that promotes the pathogenesis of PPG and the formation of Kogoj's typical spongiform pustules. The proinflammatory function of IL-36 cytokines can be further strengthened by positive feedback with the presence of IL-17/IL-23. IL-36γ expression was found to correlate with disease activity in psoriasis and is suppressed

ISSN 2721-1215 (Print), ISSN 2721-1231 (Online)
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by TNFα inhibition, therefore several recent therapeutic targets have been introduced based on the understanding of this mechanism. Inhibition of TNFα, IL-1 and IL-17A that stimulates the synthesis of IL-36α, IL-36β and IL-36γ in keratinocytes has the potential to disrupt inflammatory pathways in PPG and targets IL-23 grooves that regulate IL-17 synthesis which will have an effect on IL-36. On this pharmacological target, IL-36 receptor inhibitors are being evaluated for use as a treatment for PPG (Krueger et al., 2022; Li et al., 2019; Meier-Schiesser et al., 2019).

Psoriasis has a significant negative impact on the patient's quality of life due to damage to skin function, joints and psychological disorders. According to Bachelez et al, in 2022 in the United States reported that there is a link between psoriasis and other disorders such as metabolic diseases, infections, cardiovascular diseases and psychological disorders. Inpatient treatment in patients with moderate to severe psoriasis with a PASI score of >5 caused by the disease itself or the presence of other comorbidities. Research conducted by Choon et al in 2014 reported the average length of hospitalization of patients with PPG as many as 102 cases for 10 days with a range of length of hospitalization ranging from 3-44 days. In this study, patients who were hospitalized for 2-19 days with an average of 8 days of hospitalization (Bachelez et al., 2022; Choon et al., 2014; Kharawala et al., 2020; Wang et al., 2022).

Treatment of PPG is determined by the extent and severity of the disease. PPG therapy is based on the same therapeutic approach as plaque psoriasis, which uses systemic immunosuppressant agents and can be added with phototherapy. In the case of PPG without (Menter et al., 2021) *flares* topical treatments such as steroids, calcipotriene (calcipotriol) and tacrolimus may be considered as maintenance or adjunct therapy. Treatment algorithms for PPG that are being developed include cyclosporine, infliximab, topical corticosteroids and topical calcipotriene as first-line treatment options in addition to systemic prednisone. Treatments for PPG can currently be classified into biological and non-biological systemic agents. Based on (Benjegerdes et al., 2016; Rivera-Díaz et al., 2023) *the Japanese guidelines* for the management of PPG and *the Medical Board of the National Psoriasis Foundation* in 2022, the most common treatments for patients with PPG are retinoids, cyclosporine and methotrexate. Methotrexate restores the immunosuppressive function of regulatory T cells through inhibition of the rapamycin target mammalian pathway (mTOR). Cyclosporin, which is a calcineurin inhibitor, can be used for the therapy of PPG patients. Cyclosporine acts as an immunosuppressant agent through inhibition of calcineurin phosphatase signaling. Other non-biological agents that have been used for the treatment of PPG include mycophenolate mofetyl, hydroxyurea, apremilast and colchicine. Cyclosporine is the therapy of choice because it has a faster onset of work. Several biologics in Japan and Asian countries have been approved as PPG treatments including TNF inhibitors (infliximab, adalimumab, and certolizumab pegol), IL-17/IL-17R inhibitors (secukinumab, brodalumab, and ixekizumab) and IL-17R23 inhibitors (risankizumab and guselkumab) (Krueger et al., 2022; Rivera-Díaz et al., 2023).

In this study, most of the patients were given immunosuppressant therapy, namely 15 patients (65.2%), (methotrexate 11 patients (47.83%) and cyclosporin 4 patients (17.39%). Oral corticosteroids were given to 6 patients (26.1%), zinc 4 patients (17.4%), topical corticosteroids such as betamethasone, desoxymethasone and mometasone were given to 11 patients (47.8%) and *moisturizers* were given to 13 patients (56.5%). Methotrexate is effective in chronic plaque-type psoriasis and is also indicated for long-term therapy of patients with severe psoriasis including erythroderma, psoriatica and PPG. Cyclosporine is used to treat PPG patients who act as an immunosuppressant agent through inhibition of calcineurin phosphatase signaling and have side effects such as hypertension, nephrotoxicity and an increased risk of infection so that long-term use of cyclosporine is limited. Topical corticosteroids are effective in patients with mild-grade psoriasis. Topical corticosteroids in various formulations, potency and combinations are effective initial therapies given to patients with PPG. Other types of

treatment such as salicylic acid, keratolytic agents can be combined with steroid therapy to help reduce plaque with thicker scales so that the drug penetration becomes better. Long-term use of corticosteroids is avoided to prevent side effects in the form of local skin changes, tachyphylaxis and suppression of adrenal pituitary hypothalamic function.

The benefit of this study is to provide a useful understanding of the profile of GPP patients who receive treatment at Dr. Moewardi Hospital, Surakarta, Indonesia. This information is very relevant for health care providers and researchers in this area. The study also utilizes secondary data from medical records over a 5-year period so that it can inform health planning and patient care with PPG.

This study has some limitations. First, the findings of this study may not be universally applicable because they are specific to the patient population of Dr. Moewardi Hospital. Other regions may have different demographic variations, treatment patterns, and disease prevalence. Second, this study did not compare the outcomes or characteristics of PPG patients with a control group or other subtypes of psoriasis which could provide additional insights into the condition. Third, this study does not address the potential influence of comorbid conditions on PPG patients, which may be important for understanding the holistic health of individuals with PPG.

Conclusion

It was found that as many as 23 inpatients at Dr. Moewardi Hospital were diagnosed with PPG during the period of January 2018 – December 2022. The highest number of PPG inpatients in 2018 was 8 patients (34.78%) with the most gender being female and the highest age range in the age group of 41-50 years (26.5%). Patients were hospitalized for an average of 6-10 days (39.13%), most of the patients were given oral therapy in the immunosuppressant group as many as 15 patients (65.2%), corticosteroids 6 patients (26.1%), zinc 4 patients (17.4%), topical corticosteroids such as betamethasone, desoxymethasone and mometasone as many as 11 patients (47.8%) and moisturizers 13 patients (56.5%).

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