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REVIEW ARTICLE

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A narrative review of studies assessing the quality of life in patients with generalized pustular psoriasis

Payal M. Patel[1] | Stephanie N. Sanchez-Melendez[2,3] | Vinod E. Nambudiri[2,4]

[1]Department of Dermatology, Cutaneous Biology Research Center, Massachusetts General Hospital, Harvard University, Boston, Massachusetts, USA

[2]Department of Dermatology, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, USA

[3]Ponce Health Sciences University, School of Medicine, Ponce, Puerto Rico

[4]Harvard Medical School, Boston, Massachusetts, USA

Correspondence
Vinod E. Nambudiri, Brigham and Women's Hospital, Department of Dermatology, 221 Longwood Ave, Boston, MA, 02115, USA.
Email: vnambudiri@bwh.harvard.edu

Abstract

Generalized pustular psoriasis (GPP) is a clinical entity distinct from psoriasis, associated with a poor clinical prognosis, often resulting in severe systemic complications and mortality. The relapsing nature of the disease with recurrent or intermittent flares imposes a significant burden on patients' quality of life (QoL). Although inadequately studied, QoL data in GPP patients has been a recent point of investigation. We conducted a literature search on PubMed/MEDLINE using the following search terms: 'generalized pustular psoriasis' OR 'pustular psoriasis' AND 'quality of life'. We identified 12 relevant articles that provide insight into the large impact of GPP on the QoL of patients, the burden of the disease and the treatment, and the success of new treatment options in making a clinically important difference to QoL. This review illustrates a need for routine assessment of the QoL in interventional clinical trials for GPP and during physician encounters. This information can help guide clinicians on how to tailor the treatment approach from the patient's perspective or illustrate whether new therapies offer meaningful benefits to patient care as we enter an era of exciting new treatments for this challenging condition.

KEYWORDS
depression, generalized, generalized anxiety disorder, mental health, pustular flares, pustular psoriasis, pustular psoriasis, quality of life

1 | INTRODUCTION

Since it was first described in 1910, generalized pustular psoriasis (GPP) has been reclassified as a clinical entity distinct from psoriasis that carries significant morbidity and mortality.[1,2] The acute subtype of GPP typically leads to an abrupt onset of widespread painful erythematous patches or plaques, oedema and numerous coalescing sterile pustules, accompanied by fever, chills and malaise.[3] Disease complications can include hypocalcaemia, sepsis, renal failure, respiratory distress, high-output congestive heart failure, neutrophilic cholangitis or death.[3,4] In contrast, the subacute or annular form of GPP is characterized by the eruption of annular or figurate erythematous plaques with pustules and scaling, as well as pain or fever.[5] After the pustules resolve, considerable erythema and scaling may be present. The disease course of GPP can be labile with intermittent periods of dormancy and recurring flares over several years, especially without treatment.[6]

The management of GPP is challenging due to a need for standardized guidance on assessing GPP severity, variable response to available treatments and limited high-quality data on the efficacy of treatment options. Treatment is further complicated by the socioeconomic burden of GPP, as emotional stress is thought to contribute to the development of flares in GPP.[7] Knowledge regarding the impact GPP has on a patient's quality of life (QoL) is limited. Still,

Payal M. Patel and Stephanie N. Sanchez-Melendez authors contributed equally to this work.

recent publications have emerged to shed light on the impact of GPP on general health domains, social functioning and mental health of those with the condition.[4-12] Since a 2020 review article first described the existing literature on the clinical and socio-economic burden of GPP, nine new studies have assessed the impact on QoL of GPP in patients across several countries.[4-13] We sought to review these publications, as well as compile valuable QoL data from clinical trials studying the efficacy of advanced treatments in GPP over the course of their treatment.[8,11,12,14,15,16,17]

2 | METHODS

A comprehensive literature search was performed using the PubMed database with the following search terms: 'generalized pustular psoriasis' OR 'pustular psoriasis' AND 'quality of life' in November 2022. Supplementary searches were done by reviewing relevant articles cited in the literature. Two authors (PP and SS) performed the screening phase. The selection of articles was based on the following predefined inclusion criteria: diagnosis of GPP or GPP plus other types of psoriasis, and inclusion of QoL measures in the results.

In total, 12 publications were chosen for inclusion in this review. Of these, three were cross-sectional studies; one was an online self-reported survey that assesses depression, generalized anxiety disorder, flares and activities of daily living; one was a cross-sectional study that measures QoL; and seven were studies that evaluated the treatment efficacy of a drug and the impact it has on the QoL. Articles primarily studying localized GPP were excluded from the review.

3 | RESULTS

3.1 | Cross-sectional and retrospective assessment of GPP using the Dermatology Life and Quality Index (DLQI) and 36-Item Short-Form Health Survey (SF-36) version 2

Three studies utilized DLQI as their primary QoL instrument (Table 1), a widely used and validated 10 question, patient-reported measure with a scoring system between 0 and 30.[18] Higher DLQI scores signify more impairment of social functioning, activities of daily living and feelings of embarrassment due to clinical manifestations of the disease.[19] In a single-centre, retrospective chart review of 102 patients seen by the dermatology department at a hospital in Malaysia between 1989 and 2011, DLQI was recorded during the last follow-up when the patient was not experiencing an acute GPP flare.[6] This patient population had mean DLQI scores >10 across all categories, suggesting a significant impact of GPP on QoL: acute GPP (mean DLQI: 12.4; range: 1–28), subacute annular GPP (mean DLQI: 15.4; range: 15–24), localized GPP (mean DLQI: 17.3; range: 14–22) and impetigo herpetiformis (mean DLQI: 13.3; range: 5–24).[6]

Similarly, a multicentre, retrospective, longitudinal case series of 156 GPP patients who presented with a new GPP flare to dermatology departments in Turkey reported QoL outcomes using the DLQI.[10] In addition to the DLQI, the Perceived Stress Scale (PSS), a 10-item questionnaire (score 0–40), was used to evaluate stress or the extent to which a patient perceived life as being stressful over the past month, with 40 indicating the highest level of perceived stress.[20] The mean DLQI (11.4 ± 9.8) and PSS scores (19.3 ± 7.8) indicated a significant psychosocial burden of the disease regardless of the GPP clinical subtype. However, among GPP patients with a history of psoriasis, the mean DLQI score ($p = 0.049$) and joint involvement ($p = 0.016$) were higher than in GPP patients without a history of psoriasis. Of note, the mean reported DLQI in psoriasis patients in Turkey was much lower (7.03 ± 6.02)[21] than the mean reported in GPP patients with a history of psoriasis, suggesting that the combined burden of GPP and psoriasis is likely worse than either disease alone.

In contrast, another multicentre prospective, cross-sectional study from Turkey reported the internalized stigma state of psoriatic patients (GPP subset; $n = 21$) with the use of Psoriasis Internalized Stigma Scale (PISS) in association with DLQI and the Psoriasis Area and Severity Index (PASI).[22] PISS has five components that reflect the degree to which patients report alienation, stereotypical endorsements, perceived discrimination, social withdrawal and stigma resistance.[23] It is a validated and reliable scale to identify stigma with a significant correlation ($r = 0.726$) to DLQI in psoriasis patients.[23] The mean DLQI score for all patients with psoriasis was 10.9 ± 8.9, but the individual scores for GPP patients were not reported. However, DLQI was weakly correlated with PISS ($r = 0.431$, $p < 0.001$), and the mean PISS score in GPP patients ($n = 17$) was 70.6 ± 12.7, significantly greater ($p = 0.004$) than all other psoriasis variants except erythrodermic psoriasis (74.2 ± 13.2). These results reinforce a positive correlation between PISS, PASI and body surface area, suggesting that the disease severity is a key factor in determining stigma in GPP.

The SF-36 version 2 is another QoL instrument that utilizes a questionnaire to evaluate eight health-related concepts of QoL.[24] The questionnaire relies on patients' responses to a Likert-type scale, and lower scores reflect more disability and worse QoL attributed to the disease. Each individual value from the SF-36 version 2 domain is converted using linear transformation to obtain T-scores based on the national standard population (mean 50 points with 10 points standard deviation). A cross-sectional survey completed in multiple centres across Japan between 2016 to 2019 revealed QoL data for 83 Japanese GPP patients.[9] QoL scores for eight concepts were analysed in association with national standards and were then compared to data obtained from 105 patients in a previous survey conducted between 2003 and 2007 using T-scores. Five out of eight SF-36 version 2 subscales were lower than the national standard for the 2016–2019 group compared to all subscales in the 2003–2007 group. T-score improvement was noted in the general health, vitality, mental health and social functioning subscales compared to the prior respondents a decade earlier ($p < 0.05$). QoL scores for bodily

TABLE 1 Quality of Life Assessment in patients with GPP.

Publication	Study design	Population characteristics	*N*	QoL instrument	QoL outcome
Choon et al. (2014)	Single-centre retrospective chart review from 1989 to 2011	Adult-onset GPP Malay (57%), Chinese (29%), Indians (11%), Others (3%)	102 Acute GPP: 95 Subacute GPP: 3 Localized GPP: 4 Impetigo herpetiformis: 17	DLQI[a] when patient was out of acute GPP during the last follow up	Mean DLQI in GPP subtype (*n*) Acute GPP (95): 12.4 (*r* 1–28) Subacute GPP (3): 15.0 (*r* 15–24) Localized GPP (4): 17.3 (*r* 14–22) Impetigo herpetiformis (17): 13.3 (*r* 5–24)
Alpsoy et al. (2017)	Multicentre, prospective, cross-sectional study	Psoriasis patients in Turkey	Psoriasis: 1485 GPP patients: 21	DLQI, PISS	Mean DLQI: 10.9 ± 8.9 (not GPP specific) Mean PISS GPP patients: 70.6 ± 12.7 DLQI weakly correlated with PISS ($r = 0.431$, $p < 0.001$)
KaraPolat et al. (2022)	Multicentre retrospective, longitudinal case series	GPP patients in Turkey	156 Acute GPP: 84 GPP of pregnancy: 14 Infantile or juvenile GPP: 25 Annular GPP: 13 Mixed GPP: 20	DLQI and PSS	Mean DLQI: 11.4 ± 9.8 Mean PSS:19.3 ± 7.8
Hayama et al. (2022)	Nationwide cross-sectional survey	Japanese GPP patients	2016–2019 group: $n = 83$ compared to data 2003–2007: $n = 105$	SF36v2	2016–2019: low scores in 5/8 subscales: physical functioning, role-physical, bodily pain, general health and role-emotional 2003–2007: low scores 8/8 subscales All subscales except bodily pain were statistically significantly improved in the 2016–2019 group

Abbreviations: GPP, generalized pustular psoriasis; DLQI, Dermatology Life and Quality Index; PSS, Perceived Stress Scale-10; PISS, Psoriasis Internalized Stigma Scale; QoL, quality of life; *r*, range; SF-36v2, 36-Item Short-Form Health Survey version 2.

[a]DLQI scored 0–30 (> 10 signifies large impact to QoL); SF-36 scored 0–100 (0 represents maximum health impairment, worst; 100 represents no health impairment, best).

pain, role-physical and role-emotional domains remained very low despite substantial improvement in overall QoL. Hayama et al.[9] attributed this improvement in QoL to the recent approval of biologics and granulocyte and monocyte adsorption apheresis.

3.2 | Assessment of mental health co-morbidities and GPP flares

Several of the prior studies examining QoL above reported high mean durations and frequency of hospital admissions and pustular flares in patients with acute GPP.[6,10] An online survey documenting the experience of these GPP flares and how the disease impacted activities of daily living offered valuable insight into patient perspective. Sixty-six adults with GPP living in the United States in August 2020 completed the survey. Mental health co-morbidities such as depression and generalized anxiety disorder were reported in 42.5% and 36.4% of the respondents respectively.[7] A total of 27.3% of these patients reported not working due to disability. All participants describe at least one flare in the past 12 months and a significant change in mood during flares. Almost half of the patients responded feeling that their physicians lack understanding of the physical, emotional or psychological pain of GPP. More than half expressed hopelessness with worsening GPP or worried the condition would worsen with age.[7]

When experiencing a flare, half of the respondents also expressed a high impact of GPP on their ability to exercise, be intimate with their partner, perform errands, wear shoes or socialize with family, friends or neighbours. Almost a quarter continued to experience some of these restrictions even when not experiencing the symptoms of a flare. Notably, 70% of these patients also reported co-morbid plaque psoriasis, which may have affected survey results due to confusing terminology and the self-reported nature of the responses. Regardless, these results illustrate the need for a treatment approach that addresses the unmet needs of patients with GPP.

3.3 | Quality of life improvement in GPP with drug therapies

Frequent life-threatening flares and hospitalizations contribute to the clinical burden GPP places on patients. There are limited options for safe and efficient treatments, with many cases representing a moderate-to-severe disease recalcitrant to drugs. Numerous studies have demonstrated clinical improvement after trials with alternative therapeutic options targeting different modulators involved in immunopathogenesis, improving patients' QoL. This section will discuss various drug therapies correlated with clinical and QoL improvement.

The SF-36 has two components focused on the physical and mental dimensions of health: Physical Component Summary (PCS) and Mental Component Summary (MCS). Both scales go up to 100; the higher the score better the outcome (less impairment in health).[24] Another tool used to measure QoL improvement in patients with skin disease is the SKINDEX-29.[25-27] It is a 29-item questionnaire based on three domains: symptoms, emotions and functioning, which inquires how often during the past 4 weeks the patient experienced the effect described per item. The domains and overall score are based on a 100-point scale, and higher levels indicate that the effect is felt more often. Additionally, the psoriasis disability index (PDI) questionnaire includes 15 items related to daily activities, work or school, personal relationships, leisure, and treatment.[28] Each PDI questionnaire item is scored from 0–3, with a maximum score of 45. Higher scores denote worse QoL.

A phase 3 multicentre, single-arm, open-label study in Japan by Honma et al. assessed the efficacy of ixekizumab therapy in patients with plaque psoriasis, erythrodermic psoriasis or GPP ($n = 91$ overall; $n = 5$ for GPP).[29] Results showed that patients who responded quickly to ixekizumab treatment had better QoL and less itchiness than patients who did not respond so quickly. From week 4 to week 12, patients achieving a DLQI (0,1), meaning no impact of disease on QoL, increased as PASI percentage improvement increased (Table 2). One of the most contributing factors to improvement in QoL for patients treated with ixekizumab was the alleviation of itch. There was a positive trend in itch relief with increasing levels of improvement in PASI. Another similar finding has been reported in phase 3 multicentre, single-arm, open-label study by Okubo et al., where the long-term efficacy and safety of ixekizumab in 13 Japanese patients with erythrodermic psoriasis ($n = 8$) or GPP ($n = 5$) were assessed.[30] The mean DLQI score improvement from baseline achieved at week 12 was maintained through week 244.[30] Both studies demonstrated that selectively targeting interleukin 17A can improve QoL by having a rapid response onset, and both identified this benefit in patients with GPP.

Guselkumab is another therapy that has been evaluated for GPP. Sano et al. published a phase 3, single-arm, open-label multicentre study from Japan. Treatment efficacy was assessed in GPP patients ($n = 21$), with lesions covering more than 80% of the body surface area.[12] The study measured QoL using DLQI and SF-36 MCS, and PCS. Results showed improvement in all health-related QoL instruments measured, and by week 52, 42.9% (3/7) of the patients achieved a DLQI score of 0 or 1. The mean DLQI scores improved from baseline 10.1 to 0.5 at week 52. Therefore, selective blockade of IL-23 with guselkumab may also benefit QoL for GPP patients.

A different treatment approach has been reported by Ikeda et al., utilizing granulocyte and monocyte apheresis (GMA). This multicentre interventional study assessed the efficacy of selective depletion of elevated neutrophil levels for moderate to severe GPP ($n = 15$; 14 completed the study).[14] The authors found that DLQI showed statistically significant improvement ($p = 0.0016$) after a course of GMA treatment. Additionally, the mean DLQI score decreased from baseline 17 to 6 following GMA treatment in GPP.

Infliximab (IFX) is a monoclonal antibody specific for tumour necrosis factor-alpha (TNF-α) that has also been used as a potential treatment for pustular psoriasis and may be associated with QoL improvement. H. Torii et al. reported a phase 3, multicentre, single-arm

TABLE 2 Studies evaluating the treatment efficacy of medications for GPP and their impact on quality of life.

Publication	Study design	Drug treatment	*N*	Population characteristics	Follow up period (weeks)	QoL instrument	Outcomes
Jiajing Lu et al. (2022)	Randomized control trial	*MTX* (control group) *Acitretin* (study groups) low dose, medium dose, high dose	54	Pustular psoriasis for >6 months	52	DLQI[a]	Not GPP specific Scores reduced after treatment: most significantly in the high dosage-acitretin group ($p < 0.05$)
Bachelez, Hervé et al. (2021)	Phase 2, multicentre, randomized, double-blind, placebo-controlled trial	*Spesolimab* randomly assigned 2:1 ratio to receive a single 900 mg IV spesolimab or placebo	53	GPP presenting with a flare in 12 countries: China, France, Germany, Japan, Korea, Malaysia, Singapore, Switzerland, Taiwan, Thailand, Tunisia, United States	12	DLQI	GPP specific Median absolute change from baseline: Week 4: decreased 10 points Week 12: decreased 12.5 points
Honma et al. (2020)	Phase 3 multicentre, single-arm, open-label study	*Ixekizumab* 160 mg sc once at week 0 80 mg sc every 2 weeks through week 12	91	Plaque psoriasis (78) Erythrodermic psoriasis (8) GPP (5) Japanese patients	52	DLQI	Not GPP specific Week 0: DLQI (0, 1) rate highest for patients with PASI percentage improvement of 100, followed by 90 ≤ PASI <100, 75 ≤ PASI, <90, PASI <75 Week 12: DLQI (0,1) rate increased in all PASI groups
Okubo et al. (2019)	Phase 3, multicentre, single-arm, open-label study	*Ixekizumab* 160 mg sc once at week 0 80 mg sc every 2 weeks through week 12 80 mg sc every 4 weeks through Week 244	13	Erythrodermic psoriasis (8) GPP (5) Japanese patients	244	DLQI	Not GPP specific Mean baseline DLQI: 9.6 ± 6.5 Week 12: 4.2 ± 6.6 Week 52: 3.8 ± 4.4 Week 244: 3.6 ± 4.8
Sano et al. (2018)	Phase 3, single-arm, open-label, multicentre study	*Guselkumab* 50 mg at weeks 0, 4 and every 8 weeks thereafter through Week 52 100 mg beginning at Week 20 every 8 weeks (if dose escalation criteria met)	21	GPP (10) Erythrodermic psoriasis (11) Conducted in Japan	52	DLQI SF-36: PCS and MCS[a]	Not GPP specific Mean baseline DLQI: 10.1 ± 6.24 Week 8: 6.2 ± 8.04 week 52: 0.5 ± 0.58 DLQI (0/1) Week 52: achieved by 42.9% (3/7) of the patients Mean baseline SF-36 PCS: 38.6 ± 18.47 Week 48: +13.5 ± 12.30 Mean baseline SF-36 MCS: 40.6 ± 12.66 Week 48: +7.3 ± 11.68
H. Torii et al. (2017)	Phase 3, multicentre, single-arm trial	*Infliximab* 10 mg/kg every 8 weeks from Weeks 0 to 32	51 (43 completed the study)	Plaque psoriasis (30) Psoriatic arthritis (8) Pustular psoriasis (7) Psoriatic erythroderma (5) Conducted in Japan	40	DLQI	Not GPP specific Mean DLQI scores: Week 0: 8.3 Week 8: 5.3 Week 24: 4.6 Week 40: 3.9 Mean DLQI change for pustular psoriasis Week 40: 9.6 ± 7.2
Ikeda et al. (2013)	Multicentre interventional study	*Granulocyte and monocyte apheresis with Adacolumn* one session every week for 5 weeks	15; 14 completed the study	Moderate to severe GPP (despite conventional therapy) with more than 10% of the patient's skin covered by pustules	8–15	DLQI	GPP specific DLQI significant improvement (p value = 0.0016), reflecting better daily function and QoL Mean change in DLQI from 17 to 6

(Continues)

TABLE 2 (Continued)

Publication	Study design	Drug treatment	N	Population characteristics	Follow up period (weeks)	QoL instrument	Outcomes
Zangrilli et al. (2008)	Case report	*Adalimumab* 40 mg sc once a Week for 72 weeks	1	GPP	72	DLQI PDI[a] SKINDEX-29[a]	GPP specific Systematic improvement in DLQI, PDI and SKINDEX-29

Abbreviations: DLQI, Dermatology Life and Quality Index; GPP, generalized pustular psoriasis; IV, intravenous; MCS, Mental Component Score; MTX, methotrexate; PASI, psoriasis area and severity index; PCS, Physical Component Score; PDI, psoriasis disability index; QoL, quality of life; sc, subcutaneous; SF-36, 36-Item Short-Form Health Survey.

Note: PDI scored 0–45 (the higher score, the higher QoL impairment).

SKINDEX-29 scored 0–100 (0 indicates no effect, 100 indicates effect experienced all the time).

[a]DLQI scored 0–30 (>10 signifies large impact on QoL); SF-36, PCS-36, MCS-36 scored 0–100 (0 represents maximum health impairment, worst; 100 represents no health impairment, best).

interventional trial based in Japan which evaluated the efficacy of dose escalation with IFX therapy in different types of psoriasis patients (plaque psoriasis $n = 31$; psoriatic arthritis $n = 8$; pustular psoriasis $n = 7$; and psoriatic erythroderma $n = 5$).[16] Results showed that mean DLQI scores improved from 8.3 at week 0 to 3.9 at week 40 in all types of psoriasis included in the study. Specifically for pustular psoriasis patients, a mean change in DLQI score at week 40 of −9.6 points was observed. These authors concluded that DLQI improved across all types of psoriasis when treated with IFX. Similarly, a case report by Zangrilli et al.[31] presented a 50-year-old patient with GPP and psoriatic arthritis treated with adalimumab, a monoclonal antibody targeting TNF-α. Measurements of impact in QoL were assessed with DLQI, PDI and SKINDEX 29, resulting in a systematic improvement after treatment.

Jiajing Lu et al.[11] performed a randomized control trial that studied 54 patients diagnosed with pustular psoriasis for more than 6 months. This study compared the efficacy of methotrexate (MTX) therapy with varying doses of acitretin and explored QoL impacts in this group. Results showed a significant reduction of DLQI scores with MTX and acitretin treatment. Specifically, when comparing the control group (MTX) and the study group (acitretin), the DLQI scores of the study group reduced significantly ($p < 0.05$) with the high-dose group improving the most. These results demonstrated that high doses of acitretin were remarkably better for improving the QoL and disease severity of pustular psoriasis patients than MTX.

Most recently, a phase 2 multicentre, randomized, control trial conducted in 12 countries evaluated the efficacy of spesolimab compared to placebo in patients with GPP flare ($n = 53$).[8] Spesolimab is a humanized anti-interleukin-36 receptor monoclonal antibody recently approved in 2022 by the FDA as the first agent to treat GPP flares in adults. The therapeutic effect can be attributed to loss-of-function mutations in the interleukin-36 receptor antagonist gene and overexpression of interleukin-36 cytokines in the GPP pathomechanism. Results showed a mean absolute improvement in DLQI scores from baseline achieved in week 4 through week 12 with a single 900 mg IV dose of spesolimab. This work adds to the growing array of studies showing that many potential therapies can improve the disease burden of GPP and have significant positive impacts on patient QoL with appropriate disease management. These studies are summarized in Table 2.

3.4 | QoL instruments in dermatology

Since Finlay and Khan first introduced the DLQI in 1994, many dermatology and disease-specific validated instruments have been developed to evaluate various health-related aspects of QoL.[18,32] DLQI is the most widely used validated measure to assess general health within dermatology and QoL depending on disease severity and treatment efficacy, making it the preferred QoL instrument for use in GPP clinical trials.[33] The popularity of DLQI can be attributed

to its brevity, ease of use and availability of translations in several languages, which facilitates comparative analysis between various populations. However, DLQI has been shown to underestimate the emotional aspect of dermatologic conditions,[34] and the addition of an emotionally oriented measure, such as SF-36 or Hospital Anxiety and Depression Scale has been recommended.[35] SF-36 is one of the most used generic and validated QoL instruments that can be applied to the general population and specific disorders.[24] SF-36 version 2 provides a more comprehensive assessment of the mental health of patients compared to DLQI and uses a better scoring system than version 1, making it easier to understand and administer, and the 5-level response scale reduces standard deviation in SF-36 role scales.[36] However, SF-36 lacks a disease-specific scale to allow correlation with clinical severity. Alternatively, SKINDEX-29 is a revised questionnaire of 29 items that allows patients to reflect on the clinical symptomatology, emotional and functional domains they experienced with longer recall periods than DLQI, providing a better grasp of overall QoL.[27] In a comparative analysis of QoL instruments in patients with mild to severe psoriasis, SKINDEX-29 showed a significant correlation with clinical severity and other QoL instruments, such as SF-36, DLQI and PDI. SKINDEX-29 exhibited minimal floor effect, demonstrating improved sensitivity to changes in QoL in mild to severe psoriasis.[37]

QoL is a complex measure and may require evaluation with a disease-specific instrument that captures clinical severity and a generic or dermatology-specific scale to evaluate the emotional and functional domains.[35]

4 | CONCLUSION

We present a structured review solely focused on the QoL of patients with GPP and pustular psoriasis, as well as the impacts of treatment on this critically important health domain. This disease causes a significant burden on the life of patients due to its severe and frequent flares, socio-economic issues and mental health impact. As the severity of the disease is a key factor in determining its impact on QoL, our review highlights the potential armamentarium of therapies such as acitretin, spesolimab, ixekizumab, guselkumab, infliximab, GMA and adalimumab to treat GPP and pustular psoriasis. Given that, in many cases, patients are recalcitrant to multiple treatment modalities, varied approaches to immunosuppression may ultimately have synergistic effects on QoL improvement through better management of this condition.

Capturing, measuring and understanding metrics of QoL used in clinical trials is essential when exploring future treatment regimens for GPP. Additionally, due to the severe and resistant nature of this disease, therapies to help patients reduce the stress that this disease causes may become an important part of therapeutic control.

An important limitation of our study is that prospective studies and randomized control trials are generally lacking for GPP. Limited data and a relatively narrow body of literature focus on QoL in GPP and pustular psoriasis. Further investigative studies regarding this topic are necessary, particularly with the emergence of targeted therapies for this condition. This information can help guide clinicians on how to tailor the treatment approach from the patient's perspective or illustrate whether new therapies offer meaningful benefits to patient care as we enter an era of exciting new treatments for this challenging condition.

AUTHOR CONTRIBUTIONS

VN, PP and SS conceptualized the project. VN, PP and SS participated in preparing the original draft. PP and SS prepared the tables. VN, PP and SS participated in the writing, review and editing the final submission. All authors have read and approved the final article.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

ORCID

Payal M. Patel https://orcid.org/0000-0002-1612-3887

REFERENCES

1. von Zumbusch LR. Psoriasis und pustulöses exanthem. *Arch Dermatol Syph*. 1909;99(1):335-346.
2. Navarini AA, Burden AD, Capon F, et al. European consensus statement on phenotypes of pustular psoriasis. *J Eur Acad Dermatol Venereol*. 2017;31(11):1792-1799.
3. Zelickson BD, Muller SA. Generalized pustular psoriasis. A review of 63 cases. *Arch Dermatol*. 1991;127(9):1339-1345.
4. 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.
5. Borges-Costa J, Silva R, Goncalves L, Filipe P, Soares de Almeida L, Marques GM. Clinical and laboratory features in acute generalized pustular psoriasis: a retrospective study of 34 patients. *Am J Clin Dermatol*. 2011;12(4):271-276.
6. Choon SE, Lai NM, Mohammad NA, Nanu NM, Tey KE, Chew SF. Clinical profile, morbidity, and outcome of adult-onset generalized pustular psoriasis: analysis of 102 cases seen in a tertiary hospital in Johor, Malaysia. *Int J Dermatol*. 2014;53(6):676-684.
7. Reisner DV, Johnsson FD, Kotowsky N, Brunette S, Valdecantos W, Eyerich K. Impact of generalized pustular psoriasis from the perspective of people living with the condition: results of an online survey. *Am J Clin Dermatol*. 2022;23(Suppl 1):65-71.
8. Bachelez H, Choon SE, Marrakchi S, et al. Trial of Spesolimab for generalized pustular psoriasis. *N Engl J Med*. 2021;385(26):2431-2440.
9. Hayama K, Fujita H, Iwatsuki K, Terui T. Improved quality of life of patients with generalized pustular psoriasis in Japan: a cross-sectional survey. *J Dermatol*. 2021;48(2):203-206.
10. 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 Eur Acad Dermatol Venereol*. 2022;36(8):1256-1265.
11. Lu J, Wang Y, Li Y, Gong Y, Ding Y, Shi Y. Comparative study on the clinical efficacy and safety of acitretin and MTX in the treatment of pustular psoriasis by TLR7/MyD88/CXCL16 pathway. *Appl Bionics Biomech*. 2022;2022:9640326-9640327.
12. Sano S, Kubo H, Morishima H, Goto R, Zheng R, Nakagawa H. Guselkumab, a human interleukin-23 monoclonal antibody in Japanese patients with generalized pustular psoriasis and erythrodermic psoriasis: efficacy and safety analyses of a 52-week, phase 3, multicenter, open-label study. *J Dermatol*. 2018;45(5):529-539.
13. Kharawala S, Golembesky AK, Bohn RL, Esser D. The clinical, humanistic, and economic burden of generalized pustular psoriasis: a structured review. *Expert Rev Clin Immunol*. 2020;16(3):239-252.
14. Ikeda S, Takahashi H, Suga Y, et al. Therapeutic depletion of myeloid lineage leukocytes in patients with generalized pustular psoriasis indicates a major role for neutrophils in the immunopathogenesis of psoriasis. *J Am Acad Dermatol*. 2013;68(4):609-617.
15. Mansouri B, Richards L, Menter A. Treatment of two patients with generalized pustular psoriasis with the interleukin-1β inhibitor gevokizumab. *Br J Dermatol*. 2015;173(1):239-241.
16. Torii H, Nakano M, Yano T, Kondo K, Nakagawa H. Efficacy and safety of dose escalation of infliximab therapy in Japanese patients with psoriasis: results of the SPREAD study. *J Dermatol*. 2017;44(5):552-559.
17. Torii H, Terui T, Matsukawa M, Takesaki K, Ohtsuki M, Nakagawa H. Safety profiles and efficacy of infliximab therapy in Japanese patients with plaque psoriasis with or without psoriatic arthritis, pustular psoriasis or psoriatic erythroderma: results from the prospective post-marketing surveillance. *J Dermatol*. 2016;43(7):767-778.
18. Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI) – a simple practical measure for routine clinical use. *Clin Exp Dermatol*. 1994;19(3):210-216.
19. Basra MK, Fenech R, Gatt RM, Salek MS, Finlay AY. The dermatology life quality index 1994-2007: a comprehensive review of validation data and clinical results. *Br J Dermatol*. 2008;159(5):997-1035.
20. Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. *J Health Soc Behav*. 1983;24:385-396.
21. Atakan N, Yazici AC, Özarmağan G, et al. TUR-PSO: a cross-sectional, study investigating quality of life and treatment status of psoriasis patients in Turkey. *J Dermatol*. 2016;43(3):298-304.
22. Alpsoy E, Polat M, FettahlıoGlu-Karaman B, et al. Internalized stigma in psoriasis: a multicenter study. *J Dermatol*. 2017;44(8):885-891.
23. Alpsoy E, Şenol Y, Temel A, Baysal G, Karakaş AA. Reliability and validity of internalized stigmatization scale in psoriasis. *Turkderm*. 2015;49:45-49.
24. Lins L, Carvalho FM. SF-36 total score as a single measure of health-related quality of life: scoping review. *SAGE Open Med*. 2016;4:2050312116671725.
25. Chren MM, Lasek RJ, Flocke SA, Zyzanski SJ. Improved discriminative and evaluative capability of a refined version of Skindex, a quality-of-life instrument for patients with skin diseases. *Arch Dermatol*. 1997;133(11):1433-1440.
26. Chren MM, Lasek RJ, Quinn LM, Mostow EN, Zyzanski SJ. Skindex, a quality-of-life measure for patients with skin disease: reliability, validity, and responsiveness. *J Invest Dermatol*. 1996;107(5):707-713.
27. Chren MM. The Skindex instruments to measure the effects of skin disease on quality of life. *Dermatol Clin*. 2012;30(2):231-236. xiii.
28. Finlay AY, Kelly SE. Psoriasis-an index of disability. *Clin Exp Dermatol*. 1987;12(1):8-11.
29. Honma M, Cai Z, Burge R, Zhu B, Yotsukura S, Torisu-Itakura H. Relationship between rapid skin clearance and quality of life benefit: post hoc analysis of Japanese patients with moderate-to-severe psoriasis treated with Ixekizumab (UNCOVER-J). *Dermatol Ther (Heidelb)*. 2020;10(6):1397-1404.
30. Okubo Y, Mabuchi T, Iwatsuki K, et al. Long-term efficacy and safety of ixekizumab in Japanese patients with erythrodermic or generalized pustular psoriasis: subgroup analyses of an open-label, phase 3 study (UNCOVER-J). *J Eur Acad Dermatol Venereol*. 2019;33(2):325-332.
31. Zangrilli A, Papoutsaki M, Talamonti M, Chimenti S. Long-term efficacy of adalimumab in generalized pustular psoriasis. *J Dermatolog Treat*. 2008;19(3):185-187.
32. Lewis V, Finlay AY. 10 years experience of the dermatology life quality index (DLQI). *J Investig Dermatol Symp Proc*. 2004;9(2):169-180.
33. Kurwa HA, Finlay AY. Dermatology in-patient management greatly improves life quality. *Br J Dermatol*. 1995;133(4):575-578.
34. Both H, Essink-Bot ML, Busschbach J, Nijsten T. Critical review of generic and dermatology-specific health-related quality of life instruments. *J Invest Dermatol*. 2007;127(12):2726-2739.
35. Both H, Essink-Bot M-L, Busschbach J, Nijsten T. Critical review of generic and dermatology-specific health-related quality of life instruments. *J Investig Dermatol*. 2007;127(12):2726-2739.
36. Turner-Bowker D, Hogue SJ. Short form 12 health survey (SF-12). In: Michalos AC, ed. *Encyclopedia of Quality of Life and Well-Being Research*. Springer Netherlands; 2014:5954-5957.
37. Fernandez-Peñas P, Jones-Caballero M, Espallardo O, García-Díez A. Comparison of Skindex-29, dermatology life quality index, psoriasis disability index and medical outcome study short form 36 in patients with mild to severe psoriasis. *Br J Dermatol*. 2012;166(4):884-887.

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