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Review Article

Biomarkers for diagnosis, disease progression, and therapeutic response in psoriasis vulgaris: A mini-review

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Abstract

Psoriasis vulgaris is a chronic immune-mediated inflammatory disease with substantial clinical, psychosocial, and public health impact. Despite advances in therapeutic options, disease management continues to rely predominantly on clinical assessment, which remains limited in its ability to detect early disease, quantify subclinical inflammation, monitor disease progression, and anticipate long-term outcomes. These limitations are further compounded by marked interindividual heterogeneity in disease course, systemic inflammatory burden, comorbidity risk, and treatment response. Although a growing body of research has identified numerous candidate biomarkers related to genetic susceptibility, epidermal pathology, immune activation, and systemic inflammation, their clinical relevance and integration into routine practice remain unclear. A comprehensive synthesis that bridges molecular biomarkers with clinically meaningful applications is therefore needed. This review critically examines the current landscape of biomarkers in psoriasis vulgaris and explores their potential roles in diagnosis, assessment of disease progression, and prediction of therapeutic response. This review discusses genetic biomarkers associated with disease susceptibility and immune pathway regulation, tissue-associated biomarkers reflecting epidermal dysfunction and local inflammatory activity, and soluble biomarkers indicative of systemic inflammation and metabolic dysregulation. By organizing existing evidence across these biomarker domains, this review seeks to highlight conceptual frameworks, unresolved challenges, and future directions for biomarker-informed psoriasis management.

Keywords: Psoriasis vulgaris, biomarkers, disease progression, therapeutic response, precision medicine

Introduction

Psoriasis vulgaris is a chronic, immune-mediated inflammatory skin disease characterized by well-demarcated erythematous plaques with overlying silvery scales, resulting from dysregulated crosstalk between genetic susceptibility, environmental triggers, epidermal barrier dysfunction, and aberrant innate and adaptive immune responses [1,2]. It affects approximately 2–4% of the global population, with an estimated 60 million individuals living with psoriasis worldwide [3]. Prevalence varies markedly across regions, ranging from <0.1% in parts of East Asia to nearly 2% in Australia and Northern Europe [2,3]. According to Global Burden of Disease estimates, psoriasis accounts for more than 5 million disability-adjusted life years, exceeding the burden of several other chronic inflammatory disorders [3]. In addition to visible skin lesions, psoriasis imposes substantial psychosocial morbidity, including impaired quality of life, stigmatization, depression, and anxiety [4].

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Psoriasis is increasingly recognized as a systemic inflammatory disease rather than a purely cutaneous condition [3]. Up to 25–30% of patients develop psoriatic arthritis, often within the first decade of skin disease, while others experience cardiovascular disease, metabolic syndrome, obesity, insulin resistance, and nonalcoholic fatty liver disease [3]. These comorbidities substantially increase long-term morbidity and mortality [4]. Importantly, subclinical systemic inflammation may precede overt clinical manifestations, highlighting the need for tools that can detect disease activity beyond visible skin involvement [5].

Early detection and accurate diagnosis are therefore critical to prevent disease progression and irreversible complications. However, diagnosis of psoriasis still relies mainly on visual clinical assessment and history, with biopsy used only when features are atypical or overlapping with other dermatoses [6]. Early, mild, or pediatric disease and skin of color particularly increase the risk of misdiagnosis and delay appropriate therapy [7]. Moreover, commonly used clinical severity indices provide limited information on underlying molecular activity and are subject to interobserver variability, reducing reproducibility and sensitivity to subclinical inflammation.

Assessment of disease progression poses additional challenges. Psoriasis shows wide interindividual variability in lesion morphology, stability, and triggers, with some patients having long-standing stable plaques and others experiencing frequent remissions and exacerbations, Koebner positivity, or strong environmental triggers [8]. Current clinical scores in psoriasis vulgaris primarily capture visible skin involvement and patient-reported impact, but do not fully reflect ongoing immunologic activation, angiogenesis, oxidative stress, or systemic metabolic dysregulation that drive chronic inflammation and tissue damage [9,10]. As a result, patients with apparently controlled skin disease may continue to harbor persistent inflammatory activity, increasing the risk of relapse and comorbidities.

Therapeutic response and long-term disease control further complicate psoriasis management. Although biologic and systemic therapies targeting tumor necrosis factor alpha (TNF-α), interleukin (IL)-17, and IL-23 pathways have transformed treatment outcomes, not all patients respond equally, and secondary loss of response remains common [11,12]. Currently, treatment selection is largely empirical, and reliable predictors of therapeutic efficacy, remission durability, or adverse effects are lacking. This trial-and-error approach delays optimal therapy, increases healthcare costs, and exposes patients to unnecessary risks.

These unmet clinical needs underscore the importance of biomarkers in the management of psoriasis. Biomarkers reflecting genetic susceptibility, epidermal pathology, immune activation, and systemic inflammation have the potential to enable earlier diagnosis, objectively monitor disease activity and progression, stratify comorbidity risk, and predict therapeutic response [11]. Advances in molecular profiling have identified numerous candidate biomarkers, including genetic variants within *PSOR* loci [13,14], tissue-based markers of keratinocyte differentiation and immune infiltration [15-17], and circulating cytokines [18], chemokines, acute-phase reactants [19–22], and metabolic mediators [23].

Despite this growing body of evidence, clinical translation remains limited. Biomarker studies are often heterogeneous, focus on isolated pathways, or evaluate single outcomes without integrating diagnostic, prognostic, and therapeutic dimensions. Differences in study design, patient populations, disease severity, comorbidity burden, and treatment exposure further contribute to inconsistent findings. Consequently, there is no unified framework to guide clinicians in selecting clinically validated, context-specific, and ready-for-routine-use biomarkers. This review synthesizes and critically evaluates current evidence on genetic, tissue-associated, and soluble biomarkers in psoriasis vulgaris, with emphasis on their clinical utility for early detection, diagnosis, assessment of disease progression, and prediction of therapeutic response.

Biomarkers for early detection and diagnostic tools

Genetic biomarker

Genetic susceptibility markers provide the earliest layer of psoriasis diagnosis by identifying individuals with an intrinsic predisposition to immune dysregulation [24]. Psoriasis arises from the convergence of antigen presentation, epidermal barrier dysfunction, and dysregulated

immune signaling, driven by multiple susceptibility loci rather than a single causative gene [1,13,25]. In individuals carrying predisposing genetic variants, environmental triggers such as infection, trauma, or psychological stress can initiate immune activation, resulting in a sustained inflammatory cytokine cascade that drives epidermal hyperproliferation and chronic inflammation [26]. Familial aggregation is well documented, with monozygotic twins demonstrating a twofold to threefold higher concordance rate than dizygotic twins, and heritability estimates exceeding 60%, highlighting a strong heritable component [1,25].

At the core of genetic risk lies the major histocompatibility complex (MHC) on chromosome 6p21.3 (**Table 1**) [13,14]. Linkage and association studies have identified nine major psoriasis vulgaris susceptibility loci (*PSORS1–PSORS9*) [1,13,25]. Among these, *PSORS1* is the strongest genetic determinant and encodes human leukocyte antigen (HLA) *Cw6* [1,13,25]. *HLA-C06:02* enhances presentation of self or microbial peptides to $CD8^+$ T cells in the skin, lowering the activation threshold of cytotoxic and resident memory T cells [13]. This results in exaggerated activation of antigen-specific T cells, early disease onset, and more severe inflammation [13]. Enhanced antigen presentation primes downstream cytokine networks, particularly the IL-23/Th17 axis, explaining the strong clinical association between *HLA-C06:02* and response to IL-12/23 blockade [27,28].

In parallel, *PSOR4* on chromosome 1q21 encodes proteins of the cornified cell envelope complex and S100 calcium-binding proteins, which regulate epidermal barrier integrity and amplify local inflammatory responses in psoriatic skin (**Table 1**) [28,29]. *PSORS4* maps to the epidermal differentiation complex, which encodes key structural proteins of the cornified envelope (e.g., LCE, IVL, SPRR, PRR9) [30]. Deletion of *LCE3B/3C* within *PSORS4* is enriched in cutaneous psoriasis and linked to an impaired barrier repair response after disruption, supporting defective cornification and barrier formation as a primary lesion in genetically susceptible skin [30]. Additional *PSOR* loci (*PSOR2–PSOR12*) further modulate immune signaling, keratinocyte biology, and cytokine responses, reinforcing the polygenic architecture of psoriasis [14,15]. *ERAP1*, which regulates peptide trimming for MHC class I presentation, further refines antigenic specificity and reinforces HLA-C–restricted immune responses [25,28].

Furthermore, nutrigenomic regulation represents an emerging diagnostic dimension in psoriasis (**Table 1**). Expression of microRNA-21 (*miR-21*) and microRNA-155 (*miR-155*) reflects inflammation-driven gene regulation and can be modulated by dietary components such as vitamin D and curcumin [23]. These microRNAs regulate immune cell activation and cytokine signaling, supporting early identification of inflammatory susceptibility in psoriasis.

Tissue-associated biomarkers

Histopathological and immunohistochemical markers directly reflect disease-specific epidermal alterations (**Table 1**) [15-17]. Keratin expression patterns are fundamental—characterized by upregulation of keratin 6 (K6) and keratin 16 (K16) and downregulation of keratin 1 (K1) and keratin 10 (K10)—that distinguish psoriatic skin from normal epidermis and identify subclinical disease in non-lesional skin [16,17]. Notably, K16 expression emerges during early lesion formation and is detectable in clinically uninvolved skin, supporting its role as a marker of preclinical disease [15].

Psoriatic tissue also demonstrates marked overexpression of antimicrobial peptides, including elafin, S100 proteins, LL-37, and human β-defensins, reflecting keratinocyte stress responses and innate immune activation [16]. Overexpression of S100 proteins (S100A7, S100A8, S100A9) and activation of toll-like receptor 4 (TLR4), particularly in guttate psoriasis, further support tissue-based diagnosis by capturing innate immune activation and dysregulation of antimicrobial peptides. In parallel, tissue cytokine profiling shows elevated TNF-α, interferon-alpha (IFN-α), IL-6, IL-8, IL-12, IL-23, and Th17-related cytokines, forming a characteristic inflammatory signature that distinguishes psoriasis from other inflammatory dermatoses [2].

Soluble biomarkers

Soluble biomarkers contribute important adjunctive information for the diagnosis and systemic assessment of psoriasis vulgaris (**Table 1**). Hematological parameters, including increased neutrophil and lymphocyte counts and elevated neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR), support systemic inflammation. However, these markers are

not specific for disease severity [31,32]. Classical inflammatory indices such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and fibrinogen further reflect the systemic inflammatory state associated with active disease [33,34]. Psoriasis is also associated with activation of coagulation pathways, evidenced by increased levels of fibrinopeptide A, prothrombin fragment 1+2, D-dimer, fibrinogen, and complement component C4, alongside reduced levels of natural anticoagulants such as protein C, plasminogen, and α2-antiplasmin [35]. Markers of oxidative and metabolic stress further complement inflammatory profiling. Elevated lipid peroxidase, total cholesterol, triglycerides, low-density lipoprotein (LDL), and very-low-density lipoprotein levels (VLDL) indicate concurrent metabolic dysregulation [33]. Increased 8-hydroxy-guanosine reflects oxidative DNA damage, while elevated adipokines are associated with enhanced Th17-mediated immune responses [2].

Circulating biomarkers complement tissue findings by providing noninvasive diagnostic indicators (**Table 1**). Persistently reduced 25-hydroxyvitamin D [25(OH)D] levels reflect impaired immunoregulation and keratinocyte differentiation [36–38], while elevated YKL-40 mirrors chronic immune activation and extracellular matrix remodeling [39]. These markers assist in distinguishing psoriasis from non-inflammatory dermatoses. Furthermore, metabolic abnormalities provide supportive diagnostic signals. Psoriasis patients consistently demonstrate a higher omega-6 to omega-3 polyunsaturated fatty acid ratio, creating a proinflammatory lipid environment that promotes cytokine production [23]. In addition, selenium levels are reduced, impairing antioxidant defenses and immune regulation, thereby contributing to disease susceptibility [23].

Table 1. Genetic, tissue-associated, and soluble biomarkers for early detection and diagnostic tools in psoriasis vulgaris

Biomarker type	Biomarker	Diagnostic relevance	Reference
Genetic biomarkers	*PSOR1* (*HLA-Cw6*)	Encodes *HLA-Cw6*; heterogeneously associated with guttate and early-onset psoriasis	[29,40]
	PSOR4	Genes regulating terminal keratinocyte differentiation	[14]
	IL23R / IL12B / IL23A	Th17 pathway activation	[28]
	NFKBIA	NF-κB signaling pathway regulation	[28]
	LCE3B/LCE3C	Epidermal barrier dysfunction	[28]
	IFIH1	Type I interferon induction and innate immune activation	[28]
	DEFB4	Encodes human β-defensins 2, 3, and 4	[28]
	TNF-α polymorphisms	Associated with juvenile-onset psoriasis and psoriatic arthritis	[28]
Tissue-associated biomarkers	K16 ↑, K6 ↑	Early and disease-specific epidermal hyperproliferation	[23]
	K1 ↓, K10 ↓	Impaired terminal keratinocyte differentiation	[15]
	Antimicrobial peptides ↑ (elafin, S100 family, LL-37, β-defensins)	Innate immune activation in keratinocytes	[16]
Soluble biomarkers	Neutrophils ↑, lymphocytes ↑, NLR ↑, PLR ↑	Supportive diagnostic markers (non–severity specific)	[31,32]
	CRP ↑, ESR ↑, fibrinogen ↑	Indicators of systemic inflammation	[34]
	Fibrinopeptide A ↑, prothrombin fragment 1+2 ↑, D-dimer ↑, fibrinogen ↑, C4 ↑	Inflammation-related coagulation activation	[35]
	Protein C ↓, plasminogen ↓, α2-antiplasmin ↓	Inflammation-associated coagulation imbalance	[35]
	Lipid peroxidase ↑, total cholesterol ↑, triglycerides ↑, LDL ↑, VLDL ↑	Inflammation and metabolic dysregulation	[33]
	8-hydroxy-guanosine ↑	Oxidative DNA damage	[2]
	Adipokines ↑	Associated with increased Th17 cytokines	[33]
	25-hydroxyvitamin D [25(OH)D] ↓	Impaired immunoregulation and keratinocyte differentiation	[36-38]

Biomarker type	Biomarker	Diagnostic relevance	Reference
	YKL-40 ↑	Chronic immune activation and extracellular matrix remodeling	[39]
	Omega-6/omega-3 polyunsaturated fatty acid ratio ↑	Proinflammatory lipid milieu promoting cytokine production	[23]
	Selenium ↓	Reduced antioxidant defense and immune regulation, contributing to disease susceptibility	[23]

25(OH)D: 25-hydroxyvitamin D; CRP: C-reactive protein; DEFB4: defensin beta 4; ESR: erythrocyte sedimentation rate; HLA-Cw6: human leukocyte antigen Cw6; IFIH1: interferon induced with helicase C domain 1; IL: interleukin; K: keratin; LCE: late cornified envelope; LDL: low-density lipoprotein; LL-37: cathelicidin antimicrobial peptide; NFKBIA: nuclear factor kappa B inhibitor alpha; NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; PSOR: psoriasis susceptibility locus; TNF-α: tumor necrosis factor-alpha; VLDL: very-low-density lipoprotein.

Biomarkers to assess disease progression

Genetic biomarkers

Disease progression is driven by cumulative activation of immune signaling pathways encoded by susceptibility genes (**Table 2**). Variants in *IL12B*, *TYK2*, and *STAT5A/B* promote Th1 polarization and interferon-γ–dominant inflammation, whereas *JAK2*, *STAT3*, and *SOCS1* sustain Th17-mediated cytokine production [41]. Concurrent activation of nuclear factor kappa B (NF-κB) pathway genes (*CARD14*, *C-REL*, *TRAF3IP2*) amplifies keratinocyte-derived inflammatory signals, reinforcing epidermal hyperplasia and lesion persistence [41]. Persistent dysregulation of *miR-21* and *miR-155* sustains inflammatory gene expression and keratinocyte hyperproliferation [42]. These microRNAs amplify cytokine signaling and immune cell activation, linking genetic and epigenetic regulation to progressive disease activity [42].

Tissue-associated biomarkers

Disease progression is characterized by sustained K16 expression, which indicates ongoing epidermal activation and is associated with active or relapsing lesions (**Table 2**) [15]. Continued suppression of K1 and K10 reflects failure of terminal differentiation [16,17]. Persistent overexpression of antimicrobial peptides, including elafin, S100 proteins, LL-37, and human β-defensins, drives keratinocyte proliferation, neutrophil recruitment, and pathological angiogenesis [16]. These markers closely parallel clinical severity and plaque chronicity.

Soluble biomarkers

Soluble biomarkers provide an objective reflection of systemic inflammation and disease burden in psoriasis vulgaris (**Table 2**). Elevated CRP, erythrocyte sedimentation rate (ESR), and fibrinogen correlate with Psoriasis Area Severity Index (PASI) scores and overall systemic inflammatory activity [19,20,34]. In active psoriasis, most proinflammatory cytokines—including TNF-α, interferon-gamma (IFN-γ), IL-12, IL-18, IL-8, IL-6, IL-22, IL-17, IL-21, TGF-β1, and vascular endothelial growth factor (VEGF)—are consistently elevated and demonstrate a positive correlation with disease severity, supporting their central role in psoriasis pathogenesis [43]. In contrast, IL-10, an anti-inflammatory cytokine, shows a negative correlation with disease severity, reflecting impaired regulatory immune mechanisms in active disease [43]. Systemic inflammatory burden increases with disease progression and is reflected by elevated high-sensitivity CRP, human beta-defensin-2, and proinflammatory cytokines (IL-6, IL-8, IL-18, IFN-γ) [2]. Serum S100A8/S100A9 and CXCL10 levels further capture immune cell trafficking and innate immune amplification [44]. Although NLR and PLR reflect systemic inflammation, the limited correlation with PASI restricts their use for fine disease-severity monitoring [31,32]. In addition, metabolic imbalance worsens with disease progression. A persistently elevated omega-6/omega-3 ratio supports arachidonic acid–derived inflammatory mediator production, while chronic selenium deficiency exacerbates oxidative stress and tissue damage [23]. These soluble metabolic markers reflect systemic inflammatory load rather than isolated skin involvement.

Table 2. Genetic, tissue-associated, and soluble biomarkers associated with disease progression in psoriasis vulgaris

Biomarker type	Biomarker	Association with progression	Reference
Genetic biomarkers	*IL23R*	Sustained Th17 pathway activation	[28]
	IL12B	Amplification of Th1/Th17 responses	[28]
	IL23A	Maintenance of IL-23/Th17 signaling	[28]
	NFKBIA	NF-κB–mediated inflammatory amplification	[28]
	TNFAIP3 (A20)	Impaired negative regulation of TNF signaling	[45]
Tissue-associated biomarkers	Persistent K16 ↑	Active or relapsing disease	[15,46]
	Persistent antimicrobial peptides ↑ (elafin, S100A7/A8/A9, LL-37)	Chronic innate immune activation	[44]
Soluble biomarkers	CRP ↑, ESR ↑, fibrinogen ↑	Correlates with PASI and systemic inflammation	[19,20,34]
	TNF-α ↑, IFN-γ ↑, IL-12 ↑, IL-18 ↑, IL-8 ↑, IL-6 ↑, IL-22 ↑, IL-17 ↑, IL-21 ↑, TGF-β1 ↑, VEGF ↑	Positive correlation with disease severity	[43]
	IL-10 ↓	Negative correlation with disease severity, reflecting impaired immune regulation	[43]
	CRP ↑, human beta-defensin-2 ↑	Increase with disease progression and systemic inflammatory burden	[2]
	IL-6 ↑, IL-8 ↑, IL-18 ↑, IFN-γ ↑	Markers of progressive systemic inflammation	[2]
	S100A8/S100A9 ↑, CXCL10 ↑	Innate immune amplification and immune cell trafficking	[44]
	NLR ↑, PLR ↑	Reflect systemic inflammation but limited correlation with PASI	[31,32]
	Omega-6/omega-3 fatty acid ratio ↑	Promotes arachidonic acid–derived inflammatory mediator production	[23]
	25-hydroxyvitamin D [25(OH)D] ↓	Inversely associated with higher disease severity	[36-38]
	Selenium ↓	Associated with oxidative stress and progressive disease activity	[23]

25(OH)D: 25-hydroxyvitamin D; CRP: C-reactive protein; CXCL10: C-X-C motif chemokine ligand 10; ESR: erythrocyte sedimentation rate; IFN-γ: interferon-gamma; IL: interleukin; K16: keratin 16; LL-37: cathelicidin antimicrobial peptide; NFKBIA: nuclear factor kappa B inhibitor alpha; NLR: neutrophil-to-lymphocyte ratio; PASI: Psoriasis Area Severity Index; PLR: platelet-to-lymphocyte ratio; TGF-β1: transforming growth factor-beta 1; TNF-α: tumor necrosis factor-alpha; TNFAIP3 (A20): tumor necrosis factor alpha–induced protein 3; VEGF: vascular endothelial growth factor.

Biomarkers to predict therapeutic responses

Genetic biomarkers

*HLA-C*06:02* predicts a favorable response to ustekinumab, supporting IL-12/23 pathway dependence in genetically defined subgroups (**Table 3**) [27]. *TNFAIP3* polymorphisms, a negative regulator of NF-κB signaling, alter the magnitude of inflammatory suppression achieved with TNF-α inhibitors [45]. Polymorphisms in *IL23R* and *IL17RA* determine responsiveness to IL-23 and IL-17 blockade, directly modulating signaling through the IL-23/Th17 axis, respectively, while *ABCC1* and *ABCC2* polymorphisms affect methotrexate transport, efficacy, and toxicity by influencing intracellular transport and clearance of methotrexate [14]. Additionally, modulation of *miR-21* and *miR-155* expression in response to anti-inflammatory or nutrigenomic interventions suggests a potential role in predicting therapeutic responsiveness, particularly to vitamin D-based or diet-influenced treatment strategies [23].

Tissue-associated biomarkers

Psoriatic plaques are characterized by increased expression of proinflammatory cytokines, including TNF-α, interferon-α (IFN-α), interleukins IL-2, IL-6, IL-8, IL-12, IL-23, IL-23 receptor, and Th17-related cytokines (IL-17A and IL-22), together with elevated leukemia inhibitory factor

1 (LIF1) (**Table 3**) [2]. These mediators collectively drive keratinocyte hyperproliferation, immune cell recruitment, and sustained cutaneous inflammation [2]. Effective treatment with anthralin or anti-TNF agents results in a marked reduction of these inflammatory signals, paralleling clinical improvement [2]. Conversely, regulatory and anti-inflammatory cytokines, including IL-1, IL-4, IL-5, and IL-10, are decreased in active lesions, reflecting impaired immune regulation [2]. Partial restoration of these cytokines following anthralin and anti-TNF therapy suggests rebalancing of local immune responses [2]. In addition, lesional skin demonstrates reduced apoptosis due to increased activity of anti-apoptotic proteins, such as BCL-X, BAX, and BAK, which contribute to keratinocyte survival and plaque persistence [2]. Downregulation of these proteins after anthralin and anti-TNF treatment indicates normalization of apoptotic pathways [2]. Psoriatic keratinocytes also overexpress antimicrobial peptides, including elafin, S100 proteins, and LL-37, even in the absence of infection, reflecting persistent innate immune activation [44]. Their reduction with effective therapy further supports their role as tissue markers of treatment response [44].

Soluble biomarkers

Following therapy, most inflammatory biomarkers—including TNF-α, IFN-γ, IL-12, IL-18, IL-8, IL-17, IL-22, VEGF, TGF-β1, and pentraxin-3 (PTX3)—remain elevated, suggesting persistence of subclinical inflammation despite clinical improvement (**Table 3**) [43]. Notable exceptions include IL-10, which consistently decreases after treatment, reflecting partial restoration of regulatory immune pathways, and IL-6, which remains elevated, particularly in patients treated with psoralen plus ultraviolet A (PUVA) therapy [43]. Among all evaluated markers, CRP and IFN-γ demonstrate the strongest clinical relevance for long-term disease control, as reductions in these biomarkers are associated with longer remission duration [43]. In contrast, for other cytokines and mediators—namely TNF-α, IL-12, IL-18, IL-8, IL-17, IL-22, VEGF, IL-21, TGF-β1, and PTX3—evidence linking post-treatment biomarker levels to remission duration remains limited or unavailable [43].

Beyond conventional markers, CRP, VEGF, resistin, and CXCL10 show parallel reductions with improvement in PASI scores across biologic and systemic therapies (**Table 3**) [47]. Proteomic profiling has identified a high-performance predictive signature composed of CXCL10, MMP3, S100A8, and ACP5, which demonstrates excellent accuracy in predicting response to biologic therapy [48]. Expansion of this panel to include CCL2 further enables discrimination of response patterns among TNF-α inhibitors, IL-17–targeted agents, and methotrexate, reflecting pathway-specific immune modulation [48]. Additional immune markers, including normalization of Th1 and Th17 cell populations, further reflect effective immune modulation following anti-TNF therapy. In specific phenotypes such as generalized pustular psoriasis, decreases in procalcitonin and IL-23 levels in circulating T cells track response to anti-TNF treatment [18].

Reductions in VEGF and resistin closely parallel improvements in the PASI, indicating concurrent attenuation of angiogenesis and metabolic-inflammatory activity during effective therapy (**Table 3**) [47]. In addition, procalcitonin demonstrates a dynamic pattern characterized by elevation in active generalized pustular psoriasis followed by a marked decline after successful anti–tumor necrosis factor treatment, supporting its utility as a phenotype-specific marker for monitoring therapeutic response [49]. Additional circulating markers, including thymus and activation-regulated chemokine, platelet–lymphocyte complexes, and hematological ratios such as NLR and PLR, provide supportive information for treatment monitoring, particularly in patients receiving TNF-α inhibitors [31,32]. Metabolic and nutrigenomic soluble biomarkers complement immune monitoring. Restoration of a favorable omega-3/omega-6 polyunsaturated fatty acid ratio toward the recommended therapeutic range, reduced selenium levels, and the anti-inflammatory effects of quercetin, vitamin D, and curcumin—partly mediated through downregulation of *miRNA-21* and *miRNA-155*—highlight the contribution of metabolic pathways to disease modulation [23,50].

Table 3. Genetic, tissue-associated, and soluble biomarkers predictive of therapeutic response in psoriasis vulgaris

Biomarker type	Biomarker	Predictive value	Reference
Genetic biomarkers	*ABCC1, ABCC2*	Methotrexate transport, efficacy, and toxicity	[29]
	TNFAIP3 (A20) variants	Predict response to TNF-α inhibitors	[51]
Tissue-associated biomarkers	TNF-α ↑, IFN-α ↑, IL-2 ↑, IL-6 ↑, IL-8 ↑, IL-12 ↑, IL-23 ↑, IL-23R ↑, Th17 cytokines ↑ (IL-17A, IL-22), LIF1 ↑	Reduced following anthralin and anti-TNF therapy	[2]
	IL-1 ↓, IL-4 ↓, IL-5 ↓, IL-10 ↓	Partial restoration with anthralin and anti-TNF therapy	[2]
	Anti-apoptotic proteins (BCL-X, BAX, BAK) ↓	Modulated in response to anthralin and anti-TNF therapy	[2]
	Antimicrobial peptides ↓ (elafin, S100 proteins, LL-37)	Decrease with effective anthralin and anti-TNF therapy	[44]
Soluble biomarkers	CRP ↓, IFN-γ ↓	Predict longer remission duration	[43]
	TNF-α ↑, IL-12 ↑, IL-18 ↑, IL-8 ↑, IL-17 ↑, IL-22 ↑, VEGF ↑, TGF-β1 ↑, PTX3 ↑	Persist after therapy, indicating subclinical inflammation	[43]
	IL-10 ↓	Reflects partial restoration of regulatory immune pathways after therapy	[43]
	IL-6 ↑ (PUVA)	Remains elevated, particularly after PUVA therapy	[43]
	CRP ↓, VEGF ↓, Resistin ↓, CXCL10 ↓	Decline parallels PASI improvement across therapies	[47]
	CXCL10 ↓, MMP3 ↓, S100A8 ↓, ACP5 ↓, CCL2 ↓	Proteomic panel predicting biologic response	[48]
	Th1/Th17 cells ↓ → normalize	Reflect immune modulation after anti-TNF therapy	[52]
	CXCL10 ↓, MMP3 ↓, S100A8 ↓, ACP5 ↓, CCL2 ↓	Proteomic panel predicting biologic response	[48]
	VEGF ↓, Resistin ↓	Decline parallels PASI improvement	[47]
	Procalcitonin ↑ → ↓	Marker of generalized pustular psoriasis; decreases after successful anti-TNF therapy	[49]
	IL-23 ↑ in circulating T cells → ↓	Tracks response in generalized pustular psoriasis, response to anti-TNF therapy	[18]
	Omega-3/omega-6 fatty acid ratio	Recommended therapeutic ratio 4:1–7.5:1	[23]
	Selenium ↓	Nutritional biomarker relevant to disease modulation	[23]
	Quercetin	Anti-inflammatory effects	[50]
	Vitamin D and curcumin	Anti-inflammatory effects; ↓ miRNA-21 and miRNA-155 expression	[50]

ABCC1/ABCC2: ATP-binding cassette subfamily C member 1/2; ACP5: acid phosphatase 5; BAK: BCL-2 homologous antagonist/killer; BAX: BCL-2–associated X protein; BCL-X: B-cell lymphoma-extra large; CCL2: C-C motif chemokine ligand 2; CRP: C-reactive protein; CXCL10: C-X-C motif chemokine ligand 10; IFN-α: interferon-alpha; IFN-γ: interferon-gamma; IL: interleukin; LIF1: leukemia inhibitory factor 1; MMP3: matrix metalloproteinase 3; PASI: Psoriasis Area Severity Index; PTX3: pentraxin 3; PUVA: psoralen plus ultraviolet A; S100A8: S100 calcium-binding protein A8; Th: T helper; TNF-α: tumor necrosis factor-alpha; TNFAIP3 (A20): tumor necrosis factor alpha–induced protein 3; VEGF: vascular endothelial growth factor.

Future challenges and clinical implementation

Despite substantial progress in identifying candidate biomarkers for psoriasis, none have yet been fully integrated into routine clinical practice [53]. A major limitation is the predominance of studies with relatively small sample sizes, which restricts statistical power and limits generalizability across diverse patient populations [53]. In addition, considerable heterogeneity in study design—including differences in case definitions, disease severity, comorbidity profiles, treatment exposure, and outcome measures—has resulted in inconsistent findings. The absence

of standardized protocols for sample collection, biomarker measurement, and data interpretation further hampers comparison across studies and delays clinical translation.

Another critical challenge lies in the lack of longitudinal validation. Many proposed biomarkers demonstrate associations with disease activity or treatment response in cross-sectional analyses but lack confirmation in prospective studies that assess temporal dynamics, remission durability, and the prediction of long-term outcomes. Moreover, the clinical utility of biomarkers is often evaluated in isolation, without integration into decision-making algorithms or assessment of cost-effectiveness, accessibility, and feasibility in real-world clinical settings.

Collaborative, large-scale initiatives are essential to address these gaps. Consortia such as HIPPOCRATES provide an important framework for harmonizing methodologies, pooling multi-center data, and validating biomarkers across heterogeneous populations [54]. Such collaborative efforts enable robust stratification of disease phenotypes, systematic evaluation of biomarker performance, and alignment with clinically meaningful endpoints, including early diagnosis, prevention of disease progression, and optimization of therapeutic strategies.

Looking forward, the integration of multi-omics approaches offers a promising avenue for comprehensive disease characterization [55]. Genomic studies continue to highlight susceptibility loci and regulatory variants, including *LCE3D, IL23R, IL23A, NFKBIL1*, and *HLA-C*06:02*, which inform disease risk and immune pathway activation [45]. At the proteomic level, biomarkers such as IL-17A, IgG anti–high-density lipoprotein, GlycA, intestinal fatty acid–binding protein, and kallikrein 8 provide insight into immune activation, systemic inflammation, lipid dysfunction, and barrier integrity [55]. Emerging metabolomic candidates, including tyramine, reflect downstream metabolic alterations associated with immune dysregulation and may capture disease activity that is not detectable by conventional inflammatory markers.

Conclusion

Accumulating evidence demonstrates that biomarkers spanning genetic susceptibility, tissue pathology, and systemic inflammation provide critical insight into disease mechanisms and clinical behavior. Genetic biomarkers elucidate predisposition to immune pathways, tissue-associated markers reflect epidermal dysfunction and local inflammatory activity, and soluble biomarkers quantify systemic inflammation and treatment-induced immune modulation. Together, these biomarker classes show promise for improving early detection, monitoring disease progression, stratifying comorbidity risk, and predicting therapeutic response. Future progress depends on integrative, multi-omics approaches, large collaborative cohorts, and validation of biomarker panels linked to clinically meaningful outcomes. Incorporation of robust biomarkers into routine practice has the potential to shift psoriasis management toward precision medicine, enabling more accurate diagnosis, individualized treatment selection, and durable disease control in psoriasis vulgaris.

Ethics approval

Not required.

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Competing interests

All the authors declare that there are no conflicts of interest.

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Underlying data

Derived data supporting the findings of this study are available from the corresponding author on request.

Declaration of artificial intelligence use

We hereby confirm that no artificial intelligence (AI) tools or methodologies were utilized at any stage of this study, including during data collection, analysis, visualization, or manuscript preparation. All work presented in this study was conducted manually by the authors without the assistance of AI-based tools or systems.

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