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Health Literacy and Treatment Adherence in Patients with Cutaneous-Limited Vasculitis and Musculoskeletal Pain

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Abstract

Cutaneous-limited vasculitis (CLV) is a group of inflamed blood vessels in the skin. It often coincides with systemic symptoms, such as musculoskeletal pain, including arthralgia and myalgia. Although CLV is considered benign compared to systemic vasculitides, its chronic course, aesthetic concerns, and associated discomfort can significantly impair quality of life. Effective management typically relies on anti-inflammatory agents, corticosteroids, immunosuppressive medications, and symptom-targeted interventions. Treatment adherence is essential for symptom control and relapse prevention. However, barriers in understanding and obtaining information about a specific condition may interfere with the consistency of treatment. Health literacy is a well-established social determinant of health that may assist CLV patients with the ability to recognize disease triggers, understand reasoning for therapies, and engage in shared decision-making with their healthcare team. Patients may discontinue medications prematurely due to misinterpreting side effects or underestimating the chronic nature of the disease. Furthermore, the overlapping burden of musculoskeletal pain can exacerbate functional limitations and complicate management of the disease. Exploring the intersection between health literacy and treatment adherence in CLV can promote a more patient-centered approach by simplifying care plans and utilizing multidisciplinary teams effectively. Recognizing and addressing gaps in care and communication may enhance adherence, reduce flares, and improve long-term disease control in this under-recognized patient population.

1. INTRODUCTION

Cutaneous-limited vasculitis (CLV) is an encompassing term for a variety of inflammatory diseases involving dermal blood vessels, which vary based on vessel size, histologic features, and location. Though known for its hallmark features of palpable purpura (i.e., bleeding under the skin, causing variable-sized red-purple areas) and petechiae (i.e., a visible collection of blood under the skin, diameter of <0.5 cm), certain CLV conditions may involve musculoskeletal (MSK) symptoms [1]. Examples include urticarial vasculitis, Henoch-Schönlein Purpura, cryoglobulinemia, and microscopic polyangiitis [2]. The skin and MSK systems share common intervascular networks and immunological processes. Cutaneous vasculitis involves immune-mediated injury to the dermal microvascular unit – characterized by endothelial activation, neutrophil recruitment, and cytokine release – leading to local inflammation and tissue remodeling.

These immune signals can transfer into nearby MSK structures, which can cause systemic symptoms, such as arthralgias and myalgias, even in skin-limited disease processes [3,4]. These connected systemic symptoms are attributed to shared segmental vasculature and neurovascular reflex arcs [3,4]. Recognizing these interconnected mechanisms and their impact on patient experience emphasizes the importance of integrating clinical management

with effective, literacy-sensitive communication strategies.

To assess comprehension of a disease and management, known as health literacy, clinicians can implement protocols and screening tools to assist them in identifying gaps in care. Orthopedic literature has identified that older patients, minorities, and unemployed or low-income individuals are the most susceptible to low health literacy [5]. To facilitate communication, simple language and technology (e.g., videos demonstrating procedures and postoperative instructions) are employed to streamline patient care [5]. Health literacy plays a crucial role in patient outcomes, but it remains a widespread challenge. A landmark study by the National Assessment of Adult Literacy found that only 12% of U.S. adults had proficient health literacy, highlighting the difficulty many patients face in navigating the healthcare system [6]. Although more recent nationwide estimates are limited, this persistent gap exhibits the challenge of gauging health literacy across diverse populations. Due to its multisystemic infiltration, creating a strategic treatment plan, which may involve a combination of medications, physical therapy, and lifestyle modifications, is essential to improving quality of life (QoL). An online survey that assessed 190 patients' experience with their condition revealed that the top domains affecting their QoL were pain, physical functioning, and emotional well-being [7]. These effects implicate the importance of adherence to minimize the potentially debilitating effects of CLV. Furthermore, these strategies can be diversified by providing translation services and culturally-sensitive education. This review explores the dynamic intersection between the skin-MSK axis and health literacy in CLV. Rather than focusing solely on disease mechanisms or treatment options, it integrates how patients understand, navigate, and manage CLV alongside overlapping physical symptoms and communication barriers. By identifying current gaps in knowledge related to MSK manifestations and patient education, this review highlights the need for interdisciplinary research, clearer care strategies, and more integrated models that reflect the complexity of patient experiences.

2. METHODS

A comprehensive literature review was conducted to examine the role of health literacy and treatment adherence in patients with cutaneous-limited vasculitis (CLV) and musculoskeletal pain. This review identified relevant studies through a systematic search of PubMed, Google Scholar, and other scientific databases. Key search terms included “health literacy,” “cutaneous-limited vasculitis,” “arthralgias,” “myalgias,” “patient-centered care” and “treatment adherence,” and combinations of these keywords. The search conducted by the authors was restricted to peer-reviewed journal articles, clinical trials, literature reviews, and meta-analyses published in English from 1974 to 2025. The data synthesized by these studies provided a comprehensive understanding of CLV and related rheumatologic conditions with health literacy implications, while identifying gaps in the current research, and areas for future investigation.

2.1. Dermatological and Musculoskeletal Symptoms of Cutaneous-Limited Vasculitis

2.1.1. Pathophysiology & Typical Disease Course of CLV

The exact mechanisms of cutaneous-limited vasculitis (CLV) are not clearly delineated. However, some theories characterize the pathophysiology of this condition, such as immune complex deposition with activation of the complement system, reactions to medications, infections, and underlying autoimmune disorders [8]. The underlying pathogenesis of CLV is typically incited by a classic type III hypersensitivity reaction, where the immune system is exposed to foreign exogenous antigens, leading to immune complexes and complement activation. Complement is a system of plasma proteins and enzymes that function in innate and adaptive immunity to protect against pathogens that evade cellular contact [9]. These proteins mark pathogens for destruction through bacteriolysis, phagocytosis, and inflammatory triggers [10]. This exposure enables circulating immune complexes to deposit specifically into the walls of dermal postcapillary venules, activating the classical complement cascade [10]. This deposition and activation enable the infiltration of neutrophils and subsequent leukocytoclasia (e.g., nuclear debris resulting from neutrophil degranulation), which damages the vessel walls, ultimately resulting in the extravasation of erythrocytes from the blood vessels into the surrounding dermis [10]. Histopathology demonstrates that extravasation leakage is the

clinical manifestation of CLV and usually presents at 7 to 14 days after the initial exposure to a triggering event [10]. Importantly, this pathophysiologic process is confined to the skin, distinguishing CLV from systemic vasculitis with visceral involvement [11]. Patients will typically present with an insidious appearance of purple-red, raised lesions on the skin known as palpable purpura, measuring between 2 and 5 mm in diameter, which are occasionally accompanied by petechiae [12]. The damage to the blood vessels results in a significantly reduced blood flow, causing tissue ischemia, and potential ulceration. This suggests the size of the purpura is related to the stage of CLV. For example, acutely, CLV typically presents with small to medium-sized palpable purpura [13].

However, chronic CLV commonly presents with large ulcers or livedo reticularis, indicating a deeper systemic involvement [13]. There is notable variability in patient presentations, so there is no clear correlation with the size of the dermatologic lesion(s).

CLV usually follows a benign and self-limited course, often resolving between two to three weeks without medical intervention. Prior literature has demonstrated that CLV is idiopathic in 45-50% of cases [14]. The non-idiopathic cases are believed to be secondary to the transient nature of antigenic triggers or dysregulation of the localized immune system [15]. CLV typically resolves once the offending trigger, if not idiopathic, is identified and treated [16]. However, if CLV presents as a systemic form of vasculitis affecting multiple organs besides the skin, there is a greater possibility of recurrence [17]. Due to the high incidence of idiopathic CLV, disease management recommendations to patients can often be unclear, especially considering timing to disease resolution or recurrence.

2.1.2. Differential Diagnoses

Cutaneous-limited vasculitis (CLV) can present in several forms and may overlap with similar vasculitides, including urticarial vasculitis, leukocytoclastic vasculitis (LCV), and some malignancies. These conditions are generally limited to the dermal blood vessels and subcutaneous tissue, which typically share identical histopathologic and clinical features [18]. They often manifest as skin lesions, particularly palpable purpura, urticarial, or necrotic lesions [19]. CLV diagnosis primarily depends on analyzing the histopathology with a deep punch skin biopsy. A deep punch biopsy is preferred over a shave biopsy due to the sample size included in each test. In a deep punch biopsy, the sample will include the epidermis, superficial and deep layers of the dermis, and the superficial subcutaneous layer [20]. This allows for a thorough analysis of the lesions, given that medium-sized vessels lie above subcutaneous fat.

An accurate examination of CLV in a punch biopsy will reveal neutrophil infiltration surrounding venules and possibly show red blood cell (RBC) extravasation [21]. This exudation of RBCs indicates narrowing of the lumen of the vessel walls, causing inflammation of the skin. Additionally, direct immunofluorescence may be performed on lesions that appear within 24 to 48 hours to detect complement deposits and the presence of immunoglobulin proteins [22]. As discussed in a previous section, this deposition of complement components suggests an immune complex-mediated pathway, and can help distinguish between different subtypes of vasculitis. Additionally, although direct immunofluorescence is not always required for diagnosis, it can enhance the accuracy of diagnoses when there is a lack of clarity regarding local versus systemic involvement.

One of the most challenging differential diagnoses is urticarial vasculitis (UV), which presents as erythematous papules and plaques along with hyperpigmentation [23]. The histopathology of urticarial vasculitis involves changes in the upper dermal layer where lymphocytes, monocytes, and granulocytes circulate [24]. UV is mainly idiopathic, but a subpopulation of patients have been identified with an autoimmune etiology (Giang et al., 2018). This suggests a notable overlap with CLV with implicated immune activation through the C3a and C5a anaphylatoxins. Furthermore, anaphylatoxins bind to receptors located on mast cells and other granulocytes, inducing degranulation of these immune cells and the ensuing release of histamine. Histamine is the major inciting factor for an anaphylactic reaction, resulting in increased vascular permeability and inflammation [25]. Similar to CLV, depositions of immunoglobulin proteins, complement enzymes, or fibrinogen in blood vessel walls can be visualized by direct immunofluorescence, which can indicate UV as a type III hypersensitivity reaction [26]. Given this similarity, it is essential to consider a broader context regarding diagnosing factors, such as wheals in UV that last more than 24 hours and are

often accompanied by arthralgia [27]. In contrast, CLV remains confined to the dermis and presents with palpable papules. This provides additional evidence that the depth and size of the lesions affecting the vasculature correlate with the symptomatic presentation and aid in reaching an accurate diagnosis and prognosis.

Another differential diagnosis for CLV is LCV, which is commonly characterized as inflammation of small-sized blood vessels in the post-capillary dermal venules located in the superficial dermis [13]. Areas with venous insufficiency lead to an increase in hydrostatic pressure, especially in the lower extremities, which affects the superficial dermis. This suggests that blood vessel walls have increased permeability with venous insufficiency, so are more susceptible to immune complex deposition, ultimately resulting in inflammation. Moreover, the restriction to superficial vessels reflects the involvement of exogenous antigenic stimuli with downstream activation of transient immune triggers. As Frumholtz et al. suggest in their study, vasculitic lesions are polymorphic and multiple in number [2]. The polymorphic nature of these lesions in LCV signals a widespread involvement of the vascular process, which signifies the likelihood of continuous vascular injury. Furthermore, this implicates deposition of circulating immune complexes, which activate persistent immune-mediated pathways, such as the inflammatory classical complement cascade. This provides additional evidence of similarity to the pathogenicity of CLV. However, there are testing methods that aid clinicians in differentiating the conditions. Unlike in LCV, CLV is a clinical diagnosis and denotes the significance of ruling out systemic or autoimmune disease. It can be isolated through testing options, such as complete blood count (CBC), anti-nuclear antibody (ANA), hepatitis panels, and C3 and C4 complement levels [28]. Additionally, CLV is idiopathic in up to half of the presenting patient cases, but can occur secondary to exogenous antigenic stimuli, such as autoimmune disorders or infections.

Dissimilarly, LCV is a microscopic diagnosis primarily visualized on a skin biopsy and is less likely to be identified based on clinical manifestations alone. These distinctions highlight the importance of integrating clinical presentations with histopathology to accurately diagnose CLV.

2.1.3. Overlap with Autoimmune and Inflammatory Conditions

Vasculitis refers to a group of diseases that cause narrowing and inflammation of blood vessels, which are often involved in autoimmune disorders [29]. Autoimmune disorders occur when the body's natural defense mechanism, the adaptive immune system, misidentifies healthy tissue as foreign invaders, causing the body to damage its own blood vessel walls. As discussed previously, a key mechanism proposed for cutaneous-limited vasculitis (CLV) is a type III hypersensitivity reaction, which is mediated by an immune complex pathway [12]. This pathway is triggered by an initial exposure where T-cell lymphocytes recognize an innocuous antigen as a foreign particle, causing an immune response. This response leads to the generation of immunoglobulin G (IgG) by plasma cells. Upon subsequent exposure, IgG binds to a soluble antigen and forms free-floating immune complexes. These complexes then deposit in various tissues and activate the classical complement cascade [30]. This inflammatory cascade is one of the three distinct pathways of the complement system: classical, lectin, and alternative pathway [31]. In urticarial vasculitis (UV), activation of the classical complement pathway generates the potent anaphylatoxins C3a and C5a, promoting mast cell degeneration and histamine release [26]. Upon the release of histamine, neutrophils migrate to the vessel and undergo degranulation to release lysosomal enzymes, which perform extracellular destruction of immune complexes [32]. CLV is characterized by fibrinoid necrosis and damage to blood vessel walls and surrounding tissue [21]. This further supports the theory that CLV is an immune complex-mediated pathway. Furthermore, it provides a basis to confirm the involvement of complement activation. CLV frequently coincides with underlying autoimmune diseases, such as systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), Sjogren's syndrome, cryoglobulinemic vasculitis, and anti-neutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis (AAV) [8]. The differential diagnosis is often challenging and requires laboratory evaluation. SLE is an idiopathic chronic autoimmune disease that can affect any organ. The characteristic feature of type II or type III SLE is a malar or discoid rash, respectively. This rash resembles the red-purple lesions on the legs commonly visible with CLV. Some additional

characteristics of SLE that overlap with CLV include arthritis, arthralgia, and myalgia. Furthermore, SLE usually affects small-sized vasculature, indicating a cutaneous-limited process driven by immune dysregulation [33]. To a lesser degree, SLE can also affect medium- and large-sized vessels, suggesting a secondary entity involving a different organ, such as the lungs, kidneys, heart, or the gastrointestinal tract. SLE is characterized by a loss of tolerance to self-antigens, altered T-cell responses, and the production of autoantibodies [34]. This report implies that early complement proteins are deficient and a subsequent decrease in the clearance of immune complexes. It is important to note that due to the decreased clearance, there is an increase in vascular permeability, which enables the antigen-antibody complexes to deposit into blood vessels, and initiate the inflammatory classical complement cascade.

RA presents with a manifestation of rheumatoid nodules on the dermis, similar to the appearance of lesions in CLV [35]. This autoimmune disorder is symmetrically polyarticular with proximal migration and primarily damages the flexible synovial membrane of small joints, including the hands, elbows, and feet [15]. It can also present with pain, swelling, and an eventual loss of function in the affected joints [15]. CLV may be misdiagnosed as RA due to both conditions affecting both small- and medium-sized blood vessels, with skin rashes, discoloration, and sores, particularly surrounding the digits [36]. Pathologic features of skin-restricted RA include neutrophilic and mononuclear infiltration of blood vessels [37].

These features support the theory of increased vascular permeability and implies the occurrence of leukocytoclasia and possible necrosis. The involvement of lymphocytic penetration demonstrates the downstream effects of circulating immune complexes. Although there is overlap in the clinical manifestation of CLV and RA, it remains crucial to rule out symptoms through testing for rheumatoid factor, C-reactive protein, and anti-citrullinated proteins (ACPAs) [38]. Specifically, ACPAs are highly specific for RA, which are often used as biomarkers for the diagnosis of RA. Additionally, the dermal presentations of RA typically present in patients who have suffered from RA for several years, as opposed to a sudden occurrence of dermal lesions typically seen in CLV. These factors may help clinicians to differentiate between the two conditions despite the intersection of symptomatology.

Though rare, Sjögren's syndrome and ANCA-associated vasculitis can also coincide with CLV due to their effects on similarly sized blood vessels. Sjögren's syndrome is an autoimmune disease that particularly affects exocrine glands, but has the potential to spread to other organs. It typically manifests as a dermal rash, coinciding with the lesions seen in CLV. In this condition, there is a presence of novel autoantibodies in serum associated with vasculitis [39]. There may be a deeper systemic involvement, which may contribute to immune complex deposition and complement activation. Moreover, the association of autoantibodies with cutaneous and glandular structures suggests that the level of autoantibody titers determines whether a patient develops CLV. Similarly, Sarmiento-Monroy et al. report the strong indication of serum autoantibodies, rheumatoid factor, and antinuclear antibodies [40]. This supports that humoral immunity, rather than innate immunity, contributes to the localized pathology of CLV. Similarly, ANCA-associated vasculitis affects small vasculature and presents as purpura and skin nodules, mimicking the clinical appearance of CLV. According to a report by Hunter et al., ANCA-AAV is characterized by the formation of granulomas and inflammation of small arteries, arterioles, venules, and capillaries [41]. This suggests that a rupture of the inflamed vessels results in the diapedesis of immune cells, particularly neutrophils, ultimately giving rise to skin lesions and a purpuric rash. The presence of underlying autoimmune disorders in conjunction with classic characterizations of CLV confers an increased likelihood of recurrent CLV.

Furthermore, it highlights the importance of accurately diagnosing vasculitic skin lesions by a thorough patient history of symptoms and testing through serologic markers.

2.1.4. Burden of Musculoskeletal Pain in CLV Patients

Although cutaneous-limited vasculitis (CLV) is primarily confined to the skin, its secondary idiopathic entity can present with musculoskeletal (MSK) pain, including arthralgia (joint pain) and myalgia (muscle pain), which can impair a patient's quality of life. The pathogenesis of these MSK symptoms overlaps with components of the classical complement cascade and type III hypersensitivity. It reflects the same pathways discussed in previous sections

[12]. This immune complex-mediated inflammation blocks the laminar flow of blood through the vasculature, occluding blood vessels. Due to the resulting ischemia, the endothelial-lined vessels can no longer support the function of surrounding peripheral nerves, leading to oxygen deprivation [9]. This vasculitic neuropathy can cause sensory or motor dysfunction, ultimately presenting as pain or stiffness in joints and muscles [42]. Although joint pain is often transient, the frequent flaring of symptoms in vasculitis can damage vessels, and the muscles or organs they supply. In some cases, the pain symptoms may remain beyond the resolution of cutaneous symptoms [17]. This indicates that an ongoing systemic inflammatory response is causing musculoskeletal injury, rather than a localized structural injury.

Accordingly, systemic lupus erythematosus (SLE) is a heterogeneous autoimmune disease with a wide variety of serological presentations, implying a broad range of vascular sizes, which can be affected by this condition [43]. Furthermore, it provides additional evidence that it is a secondary entity, and the degree of severity depends on the extent to which the vessels or organs are impaired. According to Leone et al., the spectrum of involvement ranges from destruction of small vessels or a single organ, causing mild disease, to severe manifestations involving hemorrhage [34]. However, of the studies conducted, the highest prevalence of cases when CLV overlaps with SLE occurs in small vessels.

Similarly, the occurrence of CLV in patients with other connective tissue diseases, such as rheumatoid arthritis (RA), often reflects an advanced stage mediated by immune complex deposits. The lesions visible in RA mimic those seen in CLV, and are often associated with the loss of articular and periarticular bone, soft tissue inflammation, and entrapment of neuropathies, all of which contribute to pain (Krasin et al., 2022). These presentations signal the burden of systemic inflammation related to MSK degeneration, such as peripheral neuropathy or ischemia of the fingers and toes. The overload of pain symptoms has a higher manifestation in patients who have suffered from RA for over 10 years, and is particularly increased in those who test positive for serological rheumatoid factor titers (Farrow et al., 2020). This presents the significance of detecting rheumatoid autoantibodies to determine the extent of peripheral nerve involvement, which can contribute to joint pain. Additionally, according to a study conducted by Bartels & Bridges, laboratory tests that measure erythrocyte sedimentation rate or C-reactive protein may be used to support a diagnosis of CLV with systemic RA [37]. The findings presented in this section suggest that MSK pain and the resulting fatigue are major contributors to the decreased daily functionality in patients suffering from CLV. Addressing this significant burden directly may improve patient outcomes over a long-term course of treatment and, in turn, help improve their quality of life.

2.2. Current Frameworks of Health Literacy in Chronic Diseases

2.2.1. Role of Health Literacy in Chronic Disease Management

Health literacy has extensive implications for healthcare and public health, which was first utilized in the 1970s [46,47]. It is known as an individual's ability to understand and make informed decisions on their health [47,48]. Sørensen et al. illustrated that individuals with high health literacy can typically understand the factors that impact their health and make informed decisions regarding their health care [47]. Thus, an adequate level of health education improves individuals' ability to manage their health effectively, which supports the well-being of their families and communities [47,49]. Health literacy is crucial in managing chronic diseases, such as hypertension, diabetes, rheumatoid arthritis (RA), and cutaneous-limited vasculitis (CLV), as treatment adherence and active patient involvement are important for improving clinical outcomes [50]. Patients with sufficient health literacy demonstrated a higher level of comprehension of their diagnosis and the related management plan, such as adhering to their follow-up appointments, and participating in a shared decision-making process [47,50,51]. Sufficient health literacy is associated with effective symptom control and decreased hospitalization rates [52]. Whereas, limited health literacy has been correlated with suboptimal medication adherence, increased utilization of emergency and inpatient services, and diminished overall quality of life [53,54].

Patients diagnosed with CLV who present with musculoskeletal pain, who are frequently using immunosuppressant treatments, are usually recommended to be continuously monitored for symptoms and engaged in physical rehabilitation protocols [55]. Inadequate comprehension of

these therapeutic elements may contribute to nonadherence and subsequent deterioration in clinical outcomes [53]. Consequently, strengthening health literacy is critical in refining chronic disease management [56]. Therefore, patients with CLV and other chronic diseases often have a higher disease burden when the individual has lower health literacy.

2.3. Current Tools Available to Assess Health Literacy

Numerous instruments have been developed to evaluate health literacy, each grounded in distinct theoretical frameworks regarding its definition and scope [57]. These assessment tools are generally classified into two principal categories: performance-based assessments and self-report questionnaires [58]. Among the most commonly employed performance-based measures are the Test of Functional Health Literacy in Adults (TOFHLA) and the Newest Vital Sign (NVS) [59,60].

The NVS is a concise and objective tool that examines an individual's ability to interpret information on a nutrition label, thereby evaluating fundamental competencies, such as reading comprehension and numeracy [60]. Even though the tool is convenient for healthcare professionals to use, it does not assess nuances in health literacy limitations for those with low scores [58,61,62]. Meanwhile, self-report instruments – such as the European Health Literacy Survey Questionnaire (HLS-EU-Q47) and the Health Literacy Questionnaire (HLQ) – are designed to capture broader, multidimensional constructs of health literacy [58,63,64]. These encompass domains like social support, patient engagement with healthcare professionals, and an individual's ability to navigate complex health systems [58].

While valuable for identifying strengths and areas for development within a population, these tools often rely on self-perceived competencies, which may not always align with actual functional capacities [63,64]. Jessup et al. found moderate correlations between existing health literacy instruments, illustrating that these tools assess distinct dimensions of the construction [58].

This underscores the importance of selecting assessment tools that align with specific objectives, whether to evaluate functional competencies or broader aspects of health literacy [65]. Despite the availability of various validated instruments, their integration into routine clinical practice remains limited due to several persistent challenges, including [58,66]:

- Time limitations in high-demand healthcare settings.
- Insufficient training among physicians in the administration and interpretation of health literacy assessments.
- Incongruities between the cultural and linguistic characteristics of tools and the diverse backgrounds of patients.
- Stigma associated with limited literacy, which may prevent candid responses.

Jessup et al. illustrated that effective implementation required proper selection of instruments that closely corresponded to the intended measurement objective [58]. Thus, ensuring that the resulting data is reasonable for clinical decision making.

2.4. Prevalence of Low Health Literacy in Dermatology and Rheumatology Clinics

Limited health literacy is a concern that is underestimated in many settings, such as dermatology, orthopedic surgery, and rheumatology clinical settings [67]. Patients might face difficulties while comprehending medical terminology, understanding possible side effects of treatment, or understanding their disease(s) [55,68]. Literature has considerable variation in the reported prevalence of limited health literacy in rheumatology as a systematic review found a range of 7% to 42% [69]. This may be explained by differences in the study population or measurement instruments employed [69]. For example, Look et al. found that 42% of individuals with musculoskeletal disorders, such as rheumatoid arthritis (RA), showed limited health literacy, which was associated with difficulties in interpreting treatment regimens, and engaging with their health care team [69].

2.5. Available Treatments for Cutaneous Limited Vasculitis

2.5.1. Common Treatment Strategies for CLV

Cutaneous-limited vasculitis (CLV) complications are managed with a variety of therapeutic agents depending on the severity, symptoms, and inciting factor, if not idiopathic. The symptoms for early onset of CLV include inflammation, localized swelling, arthralgia, and myalgia [8]. Recognizing these clinical presentations early on guides treatment approaches and therapeutic regimens. For mildly

symptomatic and early-stage CLV, management begins with supportive measures, such as a nonsteroidal anti-inflammatory drug (NSAID), leg elevation, and refraining from prolonged standing [70]. Inhibiting cyclooxygenase (COX) enzymes is the primary mechanism of NSAIDs, which reduces both cutaneous and musculoskeletal clinical features in CLV. In cases of recurrent or persistent CLV, colchicine becomes the subsequent recommended intervention [71]. Colchicine is a distinct therapeutic agent as it offers anti-inflammatory effects through its property of microtubule inhibition, while reducing neutrophil chemotaxis and adhesion [72]. The mechanistic anti-inflammatory and microtubuleinhibition make Colchicine particularly effective in addressing musculoskeletal symptoms. However, in high-grade and severe CLV, most patients benefit from systemic corticosteroids and immunosuppressants [55,70]. Corticosteroids pharmacologically inhibit phospholipase A2, ultimately affecting the inflammatory cascade, suppressing cytokine production, and decreasing leukotrienes and prostaglandins [73]. The properties of corticosteroids make it beneficial as broad inflammatory modulators, manging cutaneous and musculoskeletal manifestations as well. If treatment is refractory to corticosteroids, then immunosuppressants are introduced Immunosuppressants – such as methotrexate, azathioprine, and cyclophosphamide – can act by suppression of lymphocyte proliferation and inhibit DNA synthesis [74]. These agents are valuable as an alternative to corticosteroids, allowing for further suppression of immune activity that exhibit dermal and arthralgic manifestations. When followed appropriately, there are a variety oftherapeutic agents with broad immunosuppressive effects that help alleviate palpable purpura, joint tenderness, swelling, and inflammation, ultimately leading to improved disease control and long-term remission. A summary of the therapeutic strategies for CLV discussed in this review is presented in Table 1.

Table 1. *Therapeutic strategies and clinical applications in the management of Cutaneous-Limited Vasculitis (CLV)*

Treatment Class	Example Agents	Mechanism of Action	Clinical Indications	Expected Outcome
NSAIDs [70]	Ibuprofen, Naproxen	Inhibit COX enzymes → ↓ prostaglandins, inflammation	Mild or early-stage CLV with musculoskeletal symptoms	Reduces inflammation, arthralgia, myalgia, and swelling
Anti-inflammatory Agent [71,72]	Colchicine	Inhibits microtubule polymerization; reduces neutrophil chemotaxis and adhesion	Recurrent or persistent CLV	Alleviates cutaneous and MSK symptoms unresponsive to NSAIDs
Corticosteroids [55,70,73]	Prednisone, Methylprednisolone	Inhibit phospholipase A2 → ↓ leukotrienes, prostaglandins, and cytokines	Moderate to severe CLV or systemic manifestations	Suppresses immune response, reduces acute flares, and supports long-term symptom control
Immunosuppressants [21,74,75]	Methotrexate, Azathioprine, Cyclophosphamide	Suppress lymphocyte proliferation or inhibit DNA synthesis	Steroid-refractory or high-grade CLV	Prevents relapse, reduces chronic inflammation, and supports disease

Abbreviations: CLV = Cutaneous-Limited Vasculitis, NSAIDs = Nonsteroidal Anti-Inflammatory Drugs, COX = Cyclooxygenase, MSK = Musculoskeletal, DNA = Deoxyribonucleic Acid

2.5.2. Scheduling of the Medication Regimens

When choosing a therapeutic agent, adherence to medication regimens is vital for efficient recovery to reduce risk of complications and recurrence of the disease. Between the different treatments for cutaneous-limited vasculitis (CLV), the scheduling of regimens varies depending on severity. Failing to maintain adherence to treatment regimens for CLV is associated with vasculitis flares [16,76]. Compliance with treatment plans is vital for optimizing long-term outcomes and improving the trajectory of clinical outcomes by minimizing future complications, such as sudden exacerbations. Additionally, studies have shown that slow tapering with systemic corticosteroids in CLV with agents, such as mycophenolate, is beneficial to prevent relapse [21,75].

In terms of chronic cases, commitment and sustained adherence to medication regimens are

especially important because CLV is prone to relapse with premature discontinuation or irregular dosing. Similarly, in a trial by Ortiz-Sanjuán et al., they demonstrated that, despite trigger withdrawal and initial therapy for CLV, ~18% of patients relapsed after five months [77]. The trial revealed that although the disease course of CLV may initially improve, long-term outcomes depend on patients and their ability to follow their treatment schedule. Thus, health literacy plays a role in a patient's ability to maintain treatment recommendations.

Discussions between healthcare providers and their patients with an appreciation of health literacy has the potential to improve adherence to treatment recommendations.

2.6. Interplay Between Health Literacy and Treatment Adherence

Understanding how patients perceive and subsequently act upon health information is essential to achieving treatment success in CLV. Health literacy is essential in shaping patients' beliefs about their disease progression and treatment [78]. In CLV, where patients may struggle with recurrent skin lesions, musculoskeletal symptoms, and fluctuating disease activity, low health literacy may create a lack of comprehension of disease chronicity, which may negatively impact adherence to the complex and multi-drug regimens patients may be recommended.

A fear of side effects, misattribution of flares, uncertainty about medication necessity, and the need for long-term management are all known barriers in low health literacy populations [79]. These may be further exacerbated by intersection factors, such as language incongruence, insurance instability, or previous negative health care encounters [53]. Patients with low health literacy may equate disease flares with medication inefficacy or adverse effects, prompting them to discontinue the medication prematurely or modify the dosage of their medication in hopes of reducing flares.

Moreover, vague terminology (e.g., 'inflammation' or 'immune suppression) may fail to convey the necessity of treatment during symptom-free periods, especially when cutaneous symptoms resolve, but joint or muscle discomfort persists. Misaligned expectations regarding the duration of treatment, interval of doses, or flare triggers can erode provider trust and increase nonadherence, resulting in diminished treatment success [80]. This is especially problematic in patients with accompanying rheumatic symptoms, who might require prolonged corticosteroid usage or chronic immunosuppressives, where adherence directly impacts disease management [81,82]. A patient's understanding of their condition and belief in the necessity of treatment are the most consistent predictors of adherence across populations with chronic diseases [79]. The biopsychosocial burden of CLV due to factors like visible skin changes, chronic pain, and fatigue takes a multifactorial toll, making it important to assess a patient's health literacy. Those with higher health literacy tend to navigate uncertainty better, seek clarification, and engage collaboratively in their care, while those with limited health literacy may default to passive and avoidant behaviors [83,84]. As reported in a study by Schillinger et al., diabetic patients with low literacy had significantly better glycemic control when providers used teach-back techniques, emphasizing that literacy-focused communication, rather than just information volume, can drive adherence to therapies [85].

These findings are relevant in CLV, where complex medication regimens and fluctuating symptoms require consistent and bidirectional provider-patient communication. Given the episodic nature of CLV, provider-patient communication must be progressive and personalized to ensure patients feel confident managing their symptoms over time.

Adherence is not merely about compliance, but also alignment between a patient's understanding and the therapeutic goals. By framing adherence as a reflection of the quality of communication between both parties rather than patient "reliability," providers can more accurately assess which barriers to patient health literacy are modifiable, and which require structural support. As Martin et al. emphasize, adherence is shaped less by the clarity of instructions and more by how well those instructions resonate with a patient's beliefs, confidence, and perceived barriers [86]. This patient-centered framing invites multidisciplinary collaboration and tools like simplified instructions, culturally relevant education, and virtual support platforms and programs, which can foster clarity for the patient. Bridging health literacy and adherence in CLV is the foundation for sustainable, long-term disease control. A summary of the different components of health literacy for CLV is presented in Table 2.

Table 2. *Health literacy definitions and examples for the management of Cutaneous-Limited Vasculitis (CLV)*

Dimension	Definition	Impact on Adherence	CLV-Specific Example
Functional Literacy [51,87]	Ability to read, interpret, and act on written or verbal health instructions.	Impacts comprehension of treatment plans, timing, and medication dosing.	Misreading corticosteroid taper instructions leading to premature taper or incorrect dosage.
Communicative Literacy [51,88]	Ability to engage in effective, two-way dialogue with healthcare providers.	Influences trust, shared decision-making, and clarification of disease course.	The patient hesitates to ask about joint pain or assumes it's unrelated, resulting in unreported flares.
Critical Literacy [51,87]	Capacity to evaluate and apply information to manage unpredictable symptoms.	Supports adaptive self-management and early recognition of disease changes.	Identifies that joint swelling is a flare and seeks medical advice rather than stopping medications.
Self-Efficacy [86,89]	Confidence in managing their health and following treatment recommendations.	Associated with treatment persistence and willingness to adhere during asymptomatic periods,	Continues immunosuppressants despite skin clearance when educated on relapse risk.
System Navigation Skills [90,91]	Ability to access care, follow referrals, and complete prescriptions.	Affects care continuity, coordination with specialists, and follow-through on monitoring.	Misses rheumatology referral for persistent arthralgia due to confusion about follow-up process.
Cultural/Language Concordance [47,92]	Health communication aligned with the patient's cultural and linguistic context.	Enhances engagement, reduces miscommunication, and builds therapeutic alliance.	Uses interpreters or visual aids to explain CLV info to non-English speaking or immigrant patients.

2.7. Strategies to Improve Adherence Through Health Literacy

2.7.1. Patient-Centered Communication Approaches for Improving Health Literacy

Patients with cutaneous-limited vasculitis (CLV) may face a complex clinical picture, including recurrent skin lesions, arthralgias, and overall systemic discomfort, which often relapses. These often chronic diseases can easily lead to misinterpretation of symptoms in patients with CLV. Health literacy can be improved in these patients with the teach-back method (asking patients to restate instructions), which has repeatedly demonstrated improved comprehension and adherence [93].

For example, randomized trials in diabetes care have found that patients exposed to teach-back had significantly higher medication and diet adherence than controls, as well as better knowledge retention and self-care skills [93]. The teach-back method has shown increased understanding of medications and follow-up instructions among low-literacy patients [93]. For CLV patients experiencing musculoskeletal pain, the teach-back method can help establish expectations, such as that pain management is part of the disease course, not a sign that treatment is failing. Furthermore, effective patient-centered communication using non-medical vocabulary and visual aids (i.e., infographics) is strongly supported by the literature [94].

Instructions delivered in language that minimizes complex medical terminology may reduce misunderstandings and dosing errors. One study found that revising pediatric medication instructions into simple language significantly reduced misinterpretations [94]. A 2024 systematic review found that video and image-based education significantly enhanced comprehension of health materials compared to text alone [95]. Improving understanding of these techniques makes patients feel more confident and engaged in their care, promoting adherence to recommended treatments. This is particularly important in patients with CLV and other chronic diseases.

2.7.2. Technological Solutions for Health Literacy

Mobile health applications offer a promising tool for improving adherence for patients managing both cutaneous vasculitis and chronic musculoskeletal symptoms. Digital health tools, such as mobile apps for education, reminders, and self-monitoring show promise for bolstering adherence and self-management in chronic diseases [96]. Meta-analyses report that smartphone apps can significantly improve medication adherence. One review of 14 trials (n

of approximately 1,800) found that app users had a moderate, statistically significant increase in adherence (effect size d of approximately 0.40) compared to usual care [96]. In cardiovascular populations, several randomized controlled trials showed that apps – often combining reminders, educational content, and feedback – led to improved adherence with improved blood pressure and lipid control [96].

Popular adherence apps, such as Medisafe, incorporate dose reminders, medication tracking, and messaging with providers, which can help patients maintain treatment goals. Beyond reminders, many apps offer disease education and symptom tracking. In cutaneous-limited vasculitis (CLV), where flares may be subtle or mistaken for unrelated skin irritation, apps that log lesion appearance and joint pain patterns can help patients recognize their disease activity consistently. These tools aid in both symptom tracking and assisting patients to differentiate between flare-ups and unrelated discomfort, a key factor in avoiding premature discontinuation of medications. Furthermore, in rheumatic disease, smartphone self-management programs have improved patients' pain self-efficacy and self-care behaviors [97]. These apps often include features for patients to log pain levels, physical activity, medication side effects, and information clinicians can share. Wearable devices and online portals similarly allow remote monitoring of symptoms (e.g., joint pain diaries or fatigue scores), reinforcing patient engagement. While rigorous evidence is still emerging, combined data indicate that well-designed apps can engage patients and nudge behavior change, mainly when they include health-literacy-friendly features like simple interfaces, audio narration, and tailored feedback [97].

2.7.3. Multidisciplinary Interventions

Managing cutaneous-limited vasculitis (CLV) may require coordination between dermatologists, rheumatologists, and primary care providers, particularly when patients present with skin lesions and arthralgias or myalgias.

These coordinated care teams can improve adherence by applying consistent and literacy-sensitive strategies across specialties. Collaborating with multiple specialists for complex chronic conditions, like vasculitis, can ensure unified messaging and tailored education at each point of care. For instance, a dermatologist may explain the role of topical steroids, while a pharmacist explains how to space doses and avoid any sort of abrupt medication discontinuation. A good example of the efficacy of the multimodal approach is in nurse-led education programs in rheumatoid arthritis – often as part of a team-based model – which have significantly improved patient outcomes. Systematic reviews report better self-care, higher satisfaction, and even enhanced medication adherence under nurse-coordinated care [98]. Pharmacist-led interventions (e.g., medication therapy management, pillbox preparation) have also been shown to boost adherence in chronic diseases by clarifying regimens and addressing concerns [99]. Multidisciplinary teams can tailor education to patient needs. For instance, providing culturally appropriate materials or using interpreters is crucial, since literacy and language barriers disproportionately affect marginalized groups.

Health literacy research emphasizes that multi-faceted, personalized interventions yield the best outcomes [100]. Successful programs often combine information-sharing – plain language handouts, teach-back, goal-setting – with active coaching and skill-building. In practice, a team might include a health educator or navigator who assesses a patient's literacy level, simplifies treatment plans, and follows up to reinforce understanding. Such integrated approaches have been linked to fewer hospital readmissions and better disease control in chronic conditions, likely because patients receive repeated, supportive teaching from multiple trusted providers.

2.7.4. Involving the Patient in Shared Decision-Making

Cutaneous-limited vasculitis (CLV) is a visually impactful and symptomatically distressing disease. Therefore, patients may have concerns about side effects, medication duration, and flare unpredictability. Shared decision-making (SDM) – engaging patients as partners in treatment choices – is a powerful adherence strategy, especially for those with limited health literacy.

In SDM, clinicians present options, including risks and benefits in understandable terms, and invite a patient’s values to guide decisions. Evidence shows that patients are more committed to the agreed plan when they participate in decisions [99]. For instance, a recent review notes that SDM physicians tend to foster better adherence because patients feel involved and invested in their care [99]. In chronic illness care, decision aids (e.g. diagrams and plain-language

summaries) have improved patient knowledge and reduced decisional conflict even among disadvantaged groups. SDM tools can empower low-literacy patients to express preferences and ask questions.

Ultimately, shared decision frameworks strengthen patient care. When patients understand why a particular medication or lifestyle change is recommended and have had input, they are more likely to follow through. For example, in cardiovascular care and hypertension management, involving patients in goal-setting and explaining the reasoning behind medications has been associated with increased adherence and trust. This is crucial in vasculitis with musculoskeletal pain, where treatment regimens (immunosuppressants, steroids) can be complex and have significant side effects. Involving patients with low health literacy means using plain language, SDM aids, visual risk charts or analogies, and checking understanding (e.g., teach-back during the decision process). When done effectively, SDM can reduce feelings of helplessness and align treatment with patients' lifestyles and goals, thereby improving adherence and outcomes [99].

3. Conclusion

Improving health literacy in rheumatologic conditions requires deliberate efforts across clinical practice, research, and medical education. One significant step is conducting prospective studies that directly link literacy screening with measurable patient outcomes, such as postoperative complications, treatment adherence, and satisfaction. These studies would provide critical evidence to support the integration of health literacy assessments into routine care. This is especially important in chronic and autoimmune conditions like cutaneous-limited vasculitis (CLV), which can appear benign, but may have further implications on patient well-being. The disease may present with persistent symptoms such as fatigue, joint pain, and skin lesions, thereby having a high demand for strong patient engagement and adherence to therapy, which are closely tied to adequate health literacy. There is also a growing need to develop health literacy tools specific to CLV that reflect the diverse populations served in orthopedics, dermatology, and rheumatology.

Generic assessments may overlook cultural nuances, language barriers, or disease-specific gaps in understanding that affect a patient's treatment adherence. While validated instruments (i.e., Newest Vital Sign, TOFHLA, and Health Literacy Questionnaire) exist, each has limitations such as time constraints, physician training gaps, cultural mismatches, and stigma, which can undermine their practical utility and patient impact. To address these barriers, medical education must incorporate training on literacy-sensitive care, equipping providers with strategies to assess comprehension, simplify communication, and tailor education to individual needs.

Incorporating these skills early in medical training can foster more inclusive, effective patient-provider interactions. By improving health literacy frameworks and aligning them with the unique burdens of chronic diseases like CLV, we can help reduce health disparities and improve outcomes. The current frameworks can move toward more equitable, patient-centered orthopedic care with advocacy efforts.

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