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Cutaneous Manifestations of Chronic Kidney Disease: A Narrative Review

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Abstract

Mucocutaneous manifestations in chronic kidney disease (CKD) are common, heterogeneous, and frequently underrecognized, spanning from xerosis and pruritus to severe entities such as calciphylaxis, as well as disorders of skin pigmentation, nail changes, and hair-growth abnormalities. Their pathophysiology reflects a convergence of epidermal barrier dysfunction, accumulation of uremic toxins, systemic inflammation, perturbations of the endogenous opioid axis, anemia, and mineral-bone disorder. Early pattern recognition improves care and guides a multimodal management strategy focused on reducing uremia through optimized dialysis and metabolic control, intensive emollient therapy and photoprotection, phototherapy, neuromodulatory agents, and—when appropriate—κ-opioid receptor modulators. Close collaboration between nephrology and dermatology, use of validated severity scales, and standardized follow-up can alleviate symptoms, lower complication rates, and potentially improve survival. Concurrently, there is a pressing need for robust cutaneous biomarkers and pragmatic trials evaluating real-world intervention bundles.

Keywords

Chronic Kidney Disease, Uremic Pruritus, Xerosis, Calciphylaxis, Cutaneous

Manifestations

1. Introduction

Mucocutaneous manifestations in chronic kidney disease (CKD) are common, heterogeneous, and frequently underdiagnosed. CKD is defined by structural or functional kidney abnormalities with a reduced glomerular filtration rate associated with persistent kidney damage for more than three months, and it is accompanied by a high burden of comorbidities, including cardiovascular disease, a systemic pro-inflammatory state, and disorders of mineral and bone metabolism [1]. As CKD progresses to advanced stages or requires renal replacement therapy—such as hemodialysis, peritoneal dialysis, or kidney transplantation—persistent uremia may favor the development of cutaneous alterations that substantially impair quality of life and, in some cases, signal potentially life-threatening complications [1] [2].

The clinical spectrum ranges from xerosis and pruritus, which are highly prevalent, to severe entities such as calciphylaxis (calcific uremic arteriolopathy). Additional findings include skin color changes characterized by pallor related to anemia, photo-exposed hyperpigmentation with a yellow-gray hue, nail and hair abnormalities, and oral findings such as xerostomia [2] [3]. In marked uremia, uremic frost may be observed, although it is now rare due to earlier initiation of dialysis [4]. These manifestations are not mere epiphenomena: uremic pruritus is associated with insomnia, depression, increased healthcare utilization, and poorer survival; calciphylaxis entails severe pain, necrotic ulcers, infections, and high mortality, **Table 1** highlights the multiple cutaneous manifestations associated with kidney disease [3]-[6].

Table 1. Extended summary of the main cutaneous abnormalities associated with chronic kidney disease (CKD).

Category	Cutaneous manifestation	Clinical description	Frequency in CKD	Main pathophysiologic mechanism
Uremia and metabolic disturbances	**Xerosis cutis (dry skin)**	Rough, scaly, poorly lubricated skin; a major substrate for uremic pruritus.	Very high (50% - 85%)	Sebaceous/eccrine gland dysfunction, impaired hydration, possible vitamin A deficiency.
	Uremic pruritus	Intense itching, localized or generalized; often worse at night and around dialysis sessions.	High (40% - 90% in dialysis)	Multifactorial: xerosis, uremic toxins, secondary hyperparathyroidism, systemic inflammation, endogenous opioid dysregulation.
	Pale-yellowish discoloration	Pallor with a yellow-brown/gray hue; **not jaundice** (sclerae remain anicteric).	Common	Anemia + dermal deposition of uremic pigments (urochromes) and carotenoids.
	Purpura and easy bruising	Ecchymoses and petechiae after minimal trauma.	Common	Capillary fragility and uremic platelet dysfunction.

Continued

Mineral and bone disorder (CKD-MBD)	**Calcinosis cutis**	Firm whitish/violaceous nodules or plaques that may ulcerate and drain chalky material.	Low-moderate	Calcium phosphate deposition in skin/subcutis; high Ca × P product and secondary hyperparathyroidism.
	Calciphylaxis (calcific uremic arteriolopathy)	Dermatologic emergency: exquisitely painful necrotic ulcers with perilesional livedo reticularis; typical sites include abdomen, thighs, and buttocks.	Low (but severe)	Calcification and thrombosis of dermal arterioles causing ischemia and necrosis.
	Prurigo nodularis	Hyperkeratotic, crusted, intensely pruritic nodules secondary to chronic scratching.	Moderate	Chronic itch-scratch cycle with repeated mechanical trauma and secondary inflammation.
Pigmentary disorders	**Hyperpigmentation (uremic melanosis)**	Diffuse brown-gray hyperpigmentation, more pronounced in photo-exposed areas.	Very common	Increased melanocyte-stimulating hormone (MSH), retention of carotenoids/uremic chromogens, dermal iron deposition.
	Hypopigmented "stellate/teardrop" macules	Scattered small hypopigmented macules, mainly on trunk and extremities.	Common	Unclear; possibly altered melanin transfer or melanocyte dysfunction.
	Half-and-half (Lindsay) nails	Proximal nail appears white (nail-bed edema/vascular changes) and distal portion is pink-brown.	Characteristic sign	Proximal nail-bed edema/vascular changes with distal pigmentary/vascular visibility; associated with uremia.
Appendageal disorders	**Diffuse alopecia**	Fine, dry, brittle hair with diffuse, non-scarring scalp hair loss.	Common	Follicular cycle disruption due to uremic/metabolic milieu and systemic inflammation/nutritional deficits.
	Brittle nails and leukonychia	Fragile nails with ridging and white discoloration/spots.	Common	Altered nail keratin formation and metabolic/nutritional disturbances.
Vascular manifestations	**Ischemic cutaneous necrosis (non-calciphylaxis)**	Necrotic skin areas, often at pressure sites, without overt calciphylaxis.	Low	Ischemia due to uremic vasculopathy and microthrombosis.
	Porphyrin-like dermatosis	Blisters, skin fragility, and hyperpigmentation on photo-exposed areas (dorsum of hands, face), resembling PCT.	Rare	Porphyrin accumulation due to impaired metabolism/excretion.
Dialysis-related	**Cysts and tumors (keratoacanthomas)**	Keratotic nodular lesions, sometimes multiple.	Higher prevalence	Altered epidermal proliferation and immune dysregulation/immunosuppression.
	Vascular access complications	Pseudoaneurysms; infections (cellulitis/abscesses); venous stenosis with limb edema.	Access-dependent	Local procedural and manipulation-related complications.
Associated/aggravated diseases	**Psoriasis**	May present de novo or worsen in the context of CKD.	Higher prevalence/severity	Complex interplay with systemic inflammation and immune dysregulation.

Continued

Bullous autoimmune diseases (pemphigus)	Increased risk of erythematous or foliaceus pemphigus.	Rare, but increased risk	Immune dysregulation linked to uremia and comorbidity burden.
Vasculitis (e.g., cryoglobulinemia)	Palpable purpura, ulcers, livedo reticularis, especially on lower limbs.	Higher risk (notably with HCV)	Immune-complex deposition and viral comorbidities.

Early identification of cutaneous signs may point to factors that accelerate renal progression or complicate management, such as disturbances of mineral and bone metabolism (hyperphosphatemia, secondary hyperparathyroidism), anemia, chronic inflammation, and suboptimal dialysis adequacy [3]. A systematic approach allows differentiation of causes, prioritization of interventions, and monitoring of response. Finally, close coordination between nephrology and dermatology is essential to implement multimodal strategies that alleviate symptoms, reduce complications, and optimize outcomes in patients with CKD [2] [3] [5].

2. Manifestations Directly Related to Uremia and Metabolic Disturbances (Uremic Dermopathy Proper)

Xerosis Cutis

Xerosis cutis is the most frequent cutaneous manifestation of CKD. Its pathophysiology is multifactorial and includes dysfunction of sebaceous and eccrine glands, increased transepidermal water loss, microinflammation inherent to the uremic state, and, in some patients, possible vitamin A deficiency [3] [7]. These mechanisms disrupt the epidermal barrier and reduce lipid content of the stratum corneum, promoting persistent dryness and neurosensory sensitization [7].

Clinically, it presents as rough, dull, scaly skin with variable pruritus. Prevalence ranges from 50% to 85% in CKD and dialysis cohorts [3] [7] [8]. Painful fissures are common on extensor surfaces (legs, forearms, dorsum of the hands, heels), facilitating secondary infection and perpetuating the itch-scratch cycle [9] [10].

Evaluation should document extent and severity, coexistence of uremic pruritus, and aggravating factors (dry climate, harsh soaps, xerogenic medications). A stepwise approach is recommended: basic skin care with highly occlusive emollients such as urea 5% - 10%, glycerin, or ammonium lactate; short baths, patdrying, and environmental humidification [11]. Education to avoid very hot water and excessive friction is essential. In refractory cases, mild keratolytics or short courses of low-potency topical corticosteroids may be added to control secondary inflammation [9]-[11]. In parallel, dialysis adequacy, hydration status, and control of comorbidities (e.g., mineral metabolism disorders) should be optimized, as correction of the uremic milieu significantly improves xerosis and associated pruritus [7].

Uremic Pruritus

Uremic pruritus is a frequent and clinically significant manifestation of CKD,

particularly in patients receiving dialysis [3]. Its pathophysiology is multifactorial, involving xerosis and barrier dysfunction, accumulation of uremic toxins (including phosphorus), secondary hyperparathyroidism with elevated PTH, persistent systemic inflammation, dysregulation of the endogenous opioid system (increased μ-opioid and decreased κ-opioid signaling), peripheral neuropathy, and possible calcium-phosphate microdeposition in the skin. These mechanisms interact with cutaneous and central neuroimmune changes, perpetuating the itch-scratch-inflammation cycle [12] [13].

Clinically, pruritus may be localized or generalized, insidious in onset, and chronic. It affects a large proportion of dialysis patients (up to 40% - 90% depending on series) and is associated with sleep disturbances, irritability, anxiety-depressive symptoms, reduced treatment adherence, and poorer quality of life. It commonly predominates on the back, arms, and face, typically without primary lesions; excoriations, lichenification, or prurigo nodularis are secondary to scratching [14] [15].

Assessment should document intensity and variability using validated scales such as the 5-D Itch, distribution, triggers, and comorbidities [16]. Alternative or concomitant causes must be excluded (eczematous dermatitis, scabies, cholestasis, thyroid disease, pruritogenic medications), and dialysis adequacy, phosphorus and PTH control, and presence of xerosis should be reviewed [12] [15] [17].

Management is stepwise and multimodal. First-line measures include barrier repair with occlusive emollients, short baths, avoidance of hot water and irritant fibers; topical menthol or capsaicin may help localized itch [17]. Second-line therapies include gabapentinoids (gabapentin/pregabalin) adjusted to GFR for neuropathic components; narrowband UVB phototherapy benefits generalized cases. Where available, opioid-axis modulators—particularly difelikefalin, a peripherally selective κ-opioid receptor agonist approved for CKD-associated pruritus in hemodialysis—can reduce itch intensity and improve symptom burden, typically administered intravenously at the end of dialysis sessions [17] [18]. Antihistamines have limited efficacy except for nocturnal sedation. In all cases, optimizing dialysis, calcium-phosphate balance, and PTH control is fundamental; sleep hygiene, stress-management techniques, and education to avoid scratching complete the approach [13] [15] [17] [19].

Pale-Yellowish Skin Discoloration

Pale-yellowish discoloration is common in CKD and results from two main mechanisms. Pallor reflects CKD-related anemia (reduced erythropoietin, functional iron deficiency, chronic inflammation), while the yellow-gray hue derives from retention of uremic pigments and carotenoids deposited in the dermis, more evident with sun exposure [3] [5] [8] [20].

Clinically, the coloration is diffuse and stable, accentuated on photo-exposed areas (face, dorsum of the hands, forearms) and palms. It often coexists with xerosis and pruritus and is not accompanied by frank jaundice or dark urine [21].

Evaluation should exclude jaundice (bilirubin, liver enzymes) and quantify ane-

mia (hemoglobin, ferritin, TSAT). Anemia correction with iron and erythropoiesis-stimulating agents per guidelines should be optimized; assess blood losses, inflammation, and nutritional deficits [20]. Improve dialysis adequacy and metabolic control (phosphorus, PTH). Recommend photoprotection and emollients to reduce dull appearance associated with xerosis. Rapid or focal color changes warrant investigation for alternative causes [3] [20] [21].

Easy Bruising and Purpura

CKD combines capillary fragility and uremic platelet dysfunction, with reduced platelet adhesion/aggregation due to uremic toxins, anemia decreasing hemodynamic support of the platelet plug, and endothelial dysfunction. Heparinization during dialysis and antiplatelet/anticoagulant drugs increase bleeding risk [3] [22].

Patients develop petechiae and ecchymoses after minimal trauma; mucosal bleeding (epistaxis, gingival bleeding) may coexist. Extensive hematomas usually require additional factors such as anticoagulation, procedures, or falls [3] [8] [23].

Initial assessment should review medications (aspirin, clopidogrel, anticoagulants) and intradialytic heparin; obtain CBC, PT/INR, aPTT, liver tests, iron indices, and dialysis adequacy; exclude vasculitis if systemic features are present. Prioritize dialysis optimization and anemia correction to improve primary hemostasis. Adjust or discontinue antithrombotic therapy when safe; individualize intradialytic heparinization. Local measures include compression and hemostatic dressings, plus education to minimize trauma. Periodic review of dialysis plans and medication burden reduces recurrence and complications [22]-[24].

Uremic Frost

Uremic frost represents superficial deposition of urea crystals on the skin from sweat in the setting of severe azotemia, classically with BUN ~200 mg/dL. It is now rare due to earlier dialysis initiation [4].

Its pathogenesis lies in the transdermal elimination of urea and other nitrogenous waste products through sweat, which crystallize on the skin surface after evaporation, forming a whitish layer resembling frost or salt. This phenomenon occurs when plasma urea concentrations exceed approximately 200 - 250 mg/dL, promoting diffusion into the sweat glands and subsequent excretion [4] [25].

Clinically, it appears as an acute fine, friable white powder or plaque on the face, neck, and trunk, leaving residue when scraped. It often coexists with xerosis and pruritus and may be confused with pityriasis versicolor or other scaly dermatoses; lack of marked erythema/inflammation and the uremic context support the diagnosis [4] [25] [26].

This condition requires urgent evaluation with metabolic profiling (BUN, creatinine, electrolytes), assessment of dialysis adequacy and volume status. Treatment is correction of uremia by initiating or intensifying dialysis, optimizing access and session duration, and hydrating according to volemia. Supportive barrier care and avoidance of excessive friction may be added. Resolution is typically rapid after uremia normalization. If plaques persist or diagnosis is uncertain, con-

sider KOH testing or dermoscopy to exclude fungal infection; empiric topical antifungals do not replace metabolic correction, which is the cornerstone of management [4] [21] [23] [25] [26].

3. Manifestations Related to Mineral and Bone Metabolism Disorders (Bone-Skin Axis)

Calcinosis Cutis

Calcinosis cutis in CKD results from deposition of calcium phosphate crystals in the dermis and subcutaneous tissue, favored by hyperphosphatemia, secondary hyperparathyroidism, and an elevated calcium-phosphate product. Local inflammation and tissue injury perpetuate precipitation and growth of deposits [6].

Clinically, it presents as hard whitish or violaceous nodules or plaques that may ulcerate and exude chalky material, with variable pain and infection risk. Distribution is often periarticular or at friction sites [3] [27].

Evaluation includes plain radiography (cloud-like or clumped calcifications), ultrasound to delineate soft tissues, and CT if needed to define extent. Mineral-bone disorder parameters (calcium, phosphorus, PTH, vitamin D) and calcium-containing medications should be reviewed [28] [29].

Management centers on correcting mineral metabolism, using non-calcium phosphate binders, dietary phosphorus restriction, adjustment of active vitamin D, and calcimimetics to control PTH, along with optimizing dialysis adequacy [27]. Sodium thiosulfate is employed as an adjuvant in calciphylaxis for its anti-calcifying (calcium chelation and increased deposit solubility), vasodilatory, and antioxidant effects, which may relieve pain and promote wound healing; it is typically administered intravenously in advanced kidney disease or hemodialysis with close monitoring for metabolic acidosis, gastrointestinal intolerance, QT prolongation, and electrolyte disturbances. Complicated lesions require advanced wound care, analgesia, and antibiotics when infected, with selective debridement considered; refractory cases may necessitate parathyroidectomy. Patient education on mechanical protection and adherence to phosphate-calcium control reduces recurrence and morbidity [6] [21] [27]-[29].

4. Pigmentary Disorders

Hyperpigmentation (Uremic Melanosis)

Diffuse hyperpigmentation in CKD is attributed to increased melanocyte-stimulating hormone (MSH) with melanocytic activation; retention of carotenoids and other uremic chromogens tinting the dermis; and, in some patients, iron/hemosiderin deposition secondary to hemolysis, transfusions, or cutaneous microbleeds. Systemic inflammation and oxidative stress of uremia may potentiate melanogenesis [3] [23] [30].

It presents as diffuse brown-gray pigmentation, more evident on photo-exposed areas (face, dorsum of the hands, forearms) and folds, often coexisting with xerosis and pruritus; jaundice is rare. Changes are gradual and symmetric; rapid,

focal, or greenish hues suggest alternative etiologies [3] [8] [30] [31].

Assessment should document distribution and severity, review pigmentogenic medications (e.g., amiodarone, minocycline), and exclude cholestasis or other causes based on clinical and laboratory findings [32]. Treatment centers on photoprotection (broad-spectrum SPF, UV-protective clothing), emollients to improve xerosis-related dullness, and metabolic optimization. In selected cases, topical depigmentation or enhanced photoprotection may be considered for marked post-inflammatory hyperpigmentation, though responses are slow and variable. Patient education regarding chronicity and skin care improves aesthetic perception and quality of life [3] [30] [31].

5. Hair and Nail Growth Disorders

"Half-and-Half" (Lindsay) Nails and Muehrcke Lines

Lindsay nails and Muehrcke lines are nail findings commonly seen in CKD and hypoalbuminemic states, respectively [33].

- Lindsay ("half-and-half") nails: the proximal nail plate appears white/opalescent due to vascular changes and nail-bed edema; the distal portion is pink-brown from increased vascular/pigment visibility. The demarcation is sharp and does not fade with pressure [34] [35].
- Muehrcke lines: paired transverse white bands reflecting hypoalbuminemia; located in the nail bed (not the plate), they do not grow with the nail and disappear with pressure [36] [37].

Differentiate from other leukonychia and complement evaluation with systemic studies (albumin, nutritional profile, CBC, dialysis adequacy); assess hepatic or cardiac comorbidities if suggested clinically. Treatment focuses on correcting hypoalbuminemia (nutritional support, treating losses, optimizing dialysis) and the underlying systemic disorder. No specific nail therapy is required; Muehrcke lines resolve with albumin normalization, and the Lindsay pattern may attenuate with metabolic and renal improvement [33] [35] [36].

Alopecia

Alopecia in CKD is multifactorial, involving protein-calorie malnutrition, uremic inflammation, thyroid and iron abnormalities, medications (antihypertensives, anticoagulants, retinoids, chemotherapeutics), and surgical/infectious stress precipitating telogen effluvium [38] [39].

Clinically, hair is fine, dry, and brittle with diffuse non-scarring loss; the scalp is usually intact, though xerosis or seborrheic dermatitis may coexist [3] [33].

Assessment should include medication and nutritional history, triggers within the prior 3 - 4 months, and targeted labs (CBC, ferritin/TSAT, TSH, vitamin D/B12/folate, dialysis adequacy) [39] [40].

Management focuses on optimizing nutrition, correcting anemia and deficiencies, treating concomitant dermatitis, and reviewing/adjusting implicated medications. Adjunctive measures include gentle shampoos, scalp emollience, cosmetic camouflage; consider topical minoxidil for prolonged effluvium if no con-

traindications. Education on reversibility and uremia control improves adherence and prognosis [39] [41] [42].

Hypertrichosis

Excess growth of fine (lanugo-type) hair, typically symmetric and gradual, predominates on the forehead, cheeks, back, and shoulders, and may coexist with xerosis and pigmentary changes [39].

Initial evaluation should review medications (steroids, cyclosporine, minoxidil), nutritional status, and dialysis adequacy. Management is primarily cosmetic (photoepilation by phototype, bleaching), with advice on photoprotection. Optimize metabolic control and comorbidities; consider psychosocial support for aesthetic impact. Systemic therapy is rarely needed; improvement of the uremic milieu may attenuate hair growth [39] [43] [44].

6. Dialysis-Specific Manifestations

Cutaneous Cysts and Tumors

In dialysis patients, epidermal cysts and keratoacanthomas are common, likely favored by immune dysregulation, cumulative UV exposure, and repetitive microtrauma [45] [46]. They present as well-defined keratotic or umbilicated papules or nodules with relatively rapid growth [45]. Management includes dermoscopic evaluation, photographic documentation, and selective excision when diagnostic doubt, bleeding, rapid growth, or functional symptoms exist. Education on photoprotection, review of photosensitizing drugs, and periodic surveillance help reduce recurrence and enable early detection of malignancy [3] [8] [21] [31].

Vascular Access Sites

Vascular access sites require systematic attention due to local complication risk [47]. Arteriovenous fistulas may develop pseudoaneurysms or venous stenosis with edema, color changes, and reduced flow; catheters are prone to infection with cellulitis or abscess formation. [48] Optimal strategy combines inspection and palpation at each session, scheduled Doppler ultrasound, strict aseptic technique, rotation of puncture sites, and early removal of unnecessary catheters. With infection, obtain cultures and start targeted antimicrobials; pseudoaneurysms, significant stenoses, or access dysfunction require endovascular or surgical intervention, prioritizing vascular capital preservation and safe dialysis continuity [47]-[49].

7. Other Findings

Nephrogenic Systemic Fibrosis (NSF) is an uncommon but clinically significant complication, primarily associated with patients with advanced chronic kidney disease (CKD), acute kidney injury, or those receiving dialysis after exposure to gadolinium-based contrast agents. Clinically, it presents with indurated, "woody" skin plaques accompanied by hyperpigmentation and a sensation of skin tightness, predominantly affecting the extremities and potentially progressing to joint contractures and functional disability; in severe cases, extracutaneous involvement may occur, including the fascia. Diagnosis is based on clinical suspicion and

can be supported by skin biopsy. Prevention is paramount, emphasizing avoidance of gadolinium when possible in advanced CKD, preference for lower-risk agents, and strict optimization of indications. Treatment is variable and includes improvement of renal function, rehabilitation, and dermatologic supportive measures, with heterogeneous clinical responses [50] [51].

8. Discussion

Cutaneous manifestations in CKD not only reflect the "uremic terrain" but also influence clinical outcomes and resource utilization [3] [30]. Pattern recognition guides decisions: refractory pruritus with xerosis mandates review of dialysis adequacy and phosphate-calcium control; painful necrotic lesions require prompt exclusion of calciphylaxis [2] [3] [6] [8]. Evidence strength is heterogeneous. For calciphylaxis, observational series and consensus dominate; management remains multimodal.[6] In CKD-associated pruritus, combined strategies integrating barrier repair, phototherapy, and neuromodulation (gabapentinoids) show benefit, with growing support for κ-opioid axis modulators in hemodialysis [7] [9] [13]. Xerostomia improves with local measures and sialogogues in selected cases [7] [9]. Important gaps persist: lack of cutaneous biomarkers reflecting uremic burden, standardization of patient-reported outcome measures (PROMs) for pruritus, and pragmatic trials evaluating intervention bundles in real-world settings [3] [8] [15] [21] [23].

9. Conclusion

The skin functions as a clinical window in CKD, enabling detection of high-impact complications, prioritization of interventions, and improvement of quality of life. Early integration of dermatology and nephrology facilitates diagnosis of severe entities such as calciphylaxis, optimizes control of pruritus and xerosis/xerostomia, and aids interpretation of color changes linked to comorbidities. A systematic approach combining updated guidelines, validated severity scales, and individualized multimodal strategies should be promoted, while stronger evidence is generated through implementation studies and pragmatic trials.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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