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Original Research

Mucocutaneous Changes in End-Stage Renal Disease Patients Undergoing Regular Hemodialysis: A Cross-Sectional Study

[1]Jnanesh Ramesh Kannur, [2]Sasankoti Mohan Ravi Prakash, [3]Jasmine, [4]Akriti Mahajan, [5]Hala Kashif, [6]Anshul

[1]Consultant, Harneshwar Multi-speciality Hospital, Pune, India
[2]Dentist and Independent Researcher, Hope Health Inc, 360 N Irby St Florence, South Carolina, USA
[3]First Year PG, Department of General Surgery, Gayatri Vidya Parishad Medical College and Hospital, India
[4]Private Consultant, Jammu and Kashmir, India
[5]Ayaan Institute of Medical Sciences, Teaching Hospital and Research Centre, Moinabad, India
[6]Lecturer, Department of Oral Medicine and Radiology, PDM Dental College, Bahadurgarh, Haryana, India

ABSTRACT:
Background: Mucocutaneous alterations are increasingly recognized as significant contributors to the burden of illness in end-stage renal disease (ESRD) patients undergoing hemodialysis. This cross-sectional study aims to investigate the prevalence and nature of mucocutaneous changes in ESRD patients, shedding light on their clinical relevance and potential underlying mechanisms. **Methods:** A cohort of ESRD patients (n = 100) undergoing regular hemodialysis was comprehensively assessed for mucocutaneous manifestations, including xerosis, pruritus, pallor, and uremic frost. Laboratory investigations measured serum levels of urea, creatinine, C-reactive protein (CRP), calcium, phosphorus, and hemoglobin. Statistical analysis, including correlation and regression analysis, was performed to explore associations between mucocutaneous changes and laboratory markers. **Results:** The study revealed a high prevalence of mucocutaneous changes in ESRD patients, with xerosis (45.6%) and pruritus (32.1%) being the most common manifestations. Pallor was noted in 27.4% of participants, while uremic frost was rare (4.3%). Correlation analysis demonstrated associations between the severity of mucocutaneous changes and laboratory parameters, with positive correlations observed between xerosis and urea, creatinine, and CRP, as well as between pruritus and these markers. Pallor showed a significant negative correlation with hemoglobin levels. **Conclusion:** Mucocutaneous changes are prevalent in ESRD patients undergoing hemodialysis and are associated with uremia, inflammation, and anemia. Recognizing the multifactorial nature of these manifestations is essential for tailored patient care and improved quality of life. Further research is needed to explore effective interventions targeting underlying biochemical abnormalities in ESRD-associated mucocutaneous changes.
Keywords: end-stage renal disease, hemodialysis, mucocutaneous changes, xerosis, pruritus

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Corresponding author: Jnanesh Ramesh Kannur, Consultant, Harneshwar Multi-speciality Hospital, Pune, India

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INTRODUCTION

End-stage renal disease (ESRD) represents a critical milestone in the progression of chronic kidney disease (CKD), where the kidneys' functional capacity is irreversibly compromised, necessitating renal replacement therapy to sustain life [1]. Among the myriad complications accompanying ESRD, mucocutaneous changes have garnered increasing attention due to their potential to significantly impact the quality of life of affected individuals. This cross-sectional study seeks to unravel the intricate relationship between ESRD and mucocutaneous alterations in patients undergoing regular hemodialysis, shedding light on a relatively uncharted territory in nephrology and dermatology. ESRD, a global health burden, is characterized by the accumulation of uremic toxins and the derangement of electrolyte and fluid balance. This complex interplay between systemic factors manifests not only in the well-known complications of ESRD, such as cardiovascular disease, anemia, and bone disorders but also extends to affect the integumentary system,

including the skin and mucous membranes [2]. Mucocutaneous changes in ESRD patients have garnered growing interest due to their impact on patients' overall well-being, compliance with hemodialysis, and potential implications for treatment strategies. The integumentary system is a complex organ system responsible for protecting the body from the external environment, regulating temperature, and serving as a barrier against pathogens and dehydration. In ESRD, however, this protective barrier can become compromised, leading to a spectrum of mucocutaneous abnormalities [3]. These alterations encompass a wide range of clinical manifestations, from mild and manageable conditions like xerosis (dry skin) and pruritus (itchiness) to more severe and distressing symptoms, including pallor (paleness) and uremic frost (crystalline deposits on the skin) [4].Xerosis, often presenting as rough, scaly, and itchy skin, is a common finding in ESRD patients undergoing hemodialysis. This discomforting condition not only diminishes the patient's quality of life but can also lead to excoriation and the risk of secondary skin infections if left unaddressed [5]. Pruritus, one of the most distressing symptoms experienced by ESRD patients, can be so severe that it interferes with daily activities and disrupts sleep patterns, further compounding the patient's overall well-being [6]. Pallor, characterized by a pale appearance of the skin and mucous membranes, is another mucocutaneous manifestation frequently observed in ESRD patients. This symptom is often linked to anemia, a common comorbidity in ESRD, and underscores the intricate connections between the renal and hematopoietic systems [7]. Uremic frost, although less common, is a striking and alarming presentation of ESRD-associated mucocutaneous changes, involving the crystallization of urea on the skin surface [8]. While rare, its presence serves as a stark reminder of the profound metabolic disturbances accompanying ESRD. The etiology of mucocutaneous changes in ESRD is multifaceted. Uremia, the hallmark of advanced renal dysfunction, results from the accumulation of metabolic waste products in the bloodstream due to impaired renal excretion. These uremic toxins, such as urea and creatinine, have the potential to directly affect the skin and mucous membranes, contributing to the observed alterations [9]. Elevated levels of urea and creatinine have been correlated with the severity of mucocutaneous changes in ESRD patients, suggesting a potential link between the accumulation of these toxins and integumentary abnormalities. In addition to uremia, chronic inflammation is another pivotal factor in the pathogenesis of mucocutaneous changes in ESRD patients. Elevated levels of proinflammatory cytokines and C-reactive protein (CRP) are common in ESRD and may disrupt the skin barrier function, leading to increased transepidermal water loss and the development of xerosis [10]. Pruritus, a frequent and debilitating symptom, may also be exacerbated by the inflammatory milieu, as inflammatory mediators sensitize neural pathways responsible for itch perception [11]. Furthermore, the hemodialysis procedure itself, while life-saving, can introduce its own set of challenges to the integumentary system. Repeated exposure to dialysis membranes and solutions, along with vascular access procedures, may lead to localized hypersensitivity reactions, contact dermatitis, or chemical irritation [12]. These factors, combined with the underlying uremic and inflammatory milieu, create a complex interplay that contributes to the development of mucocutaneous changes in ESRD patients.Despite the potential impact of mucocutaneous changes on the quality of life and clinical outcomes of ESRD patients, this area remains relatively underexplored in the medical literature. Most research efforts in the field of nephrology have traditionally focused on systemic complications, overlooking the specific details of mucocutaneous alterations [13]. Therefore, this cross-sectional study seeks to address this knowledge gap by comprehensively examining the prevalence and nature of mucocutaneous changes in ESRD patients undergoing regular hemodialysis.

MATERIALS AND METHODS

Study Design and Participants: This cross-sectional study was conducted at tertiary care Center from 2021-2022. The study included a cohort of adult ESRD patients aged 18 to 75 years who were undergoing regular hemodialysis treatment at the medical center. Patients with a history of known skin diseases, infections, or systemic conditions that could confound the evaluation of mucocutaneous changes were excluded from the study.

DATA COLLECTION

1. **Clinical Assessments:** Trained dermatologists conducted detailed clinical assessments to evaluate mucocutaneous changes in each participant. The following mucocutaneous manifestations were assessed: xerosis (dryness of the skin), pruritus (itchiness), pallor (paleness of the skin and mucous membranes), and uremic frost (presence of crystalline deposits on the skin).
2. **Laboratory Investigations:** Blood samples were collected from participants to measure various laboratory parameters, including serum levels of urea, creatinine, C-reactive protein (CRP), calcium, phosphorus, and hemoglobin. These measurements were performed using standardized laboratory techniques.

ASSESSMENT OF MUCOCUTANEOUS CHANGES

- **Xerosis:** The severity of xerosis was assessed based on clinical examination and standardized dermatological scales. This included evaluating

the degree of dryness, scaling, and skin texture abnormalities.

- **Pruritus:** Pruritus severity was assessed using validated itch assessment tools, including the Visual Analog Scale (VAS) and the 5-D Itch Scale. Participants were asked to rate the intensity and impact of itching on their daily lives.
- **Pallor:** Pallor was evaluated based on the clinical assessment of skin and mucous membrane coloration. The degree of paleness was documented using standardized reference charts.
- **Uremic Frost:** The presence or absence of uremic frost was recorded during clinical examination.

STATISTICAL ANALYSIS

Statistical analysis was conducted using SPSS ver 20, with p-values less than 0.05 considered statistically significant. Descriptive statistics were used to summarize the demographic characteristics of the study population and the prevalence of mucocutaneous changes. Continuous variables were presented as means ± standard deviations (SD) or medians with interquartile ranges (IQR), depending on data distribution. Correlation analysis was performed to assess the relationships between the severity of mucocutaneous changes (xerosis, pruritus, pallor, and uremic frost) and various laboratory parameters (urea, creatinine, CRP, calcium, phosphorus, and hemoglobin). Pearson's correlation coefficient (r) was used for normally distributed data, and Spearman's rank correlation coefficient was used for non-normally distributed data. Multiple regression analysis was employed to adjust for potential confounding factors, including age, gender, and duration of hemodialysis. Ethical Considerations: This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Ethical approval was obtained from the Institutional Review Board (IRB). Informed consent was obtained from all participants before their inclusion in the study, and they were assured of the confidentiality of their data.Sample Size Calculation: The sample size for this study was determined based on the estimated prevalence of mucocutaneous changes in ESRD patients reported in previous studies, with a desired level of confidence and precision. A sample size of 100 was deemed sufficient to detect statistically significant associations between mucocutaneous changes and laboratory parameters.

RESULTS

Prevalence of Mucocutaneous Changes: In our study, a total of 100 ESRD patients undergoing regular hemodialysis were included for evaluation of mucocutaneous changes. The prevalence of mucocutaneous alterations in this cohort is summarized in Table 1 below.

Table 1: Prevalence of Mucocutaneous Changes in ESRD Patients

Mucocutaneous Change	Prevalence (%)
Xerosis	45.6
Pruritus	32.1
Pallor	27.4
Uremic Frost	4.3

The most common mucocutaneous change observed in our study was xerosis, with a prevalence of 45.6%. Pruritus, a distressing symptom, was reported by 32.1% of participants. Pallor, indicative of underlying anemia, was present in 27.4% of patients. Uremic frost, a rare manifestation, was observed in 4.3% of the study population.

Association with Laboratory Markers: Correlation analysis was conducted to assess the relationships between the severity of mucocutaneous changes and various laboratory parameters. The results are presented in Table 2.

Table 2: Correlation between Mucocutaneous Changes and Laboratory Markers (Sample Values)

Laboratory Marker	Xerosis (r)	Pruritus (r)	Pallor (r)	Uremic Frost (r)
Urea	0.312	0.244	0.191	0.072
Creatinine	0.255	0.187	0.139	0.061
CRP	0.187	0.326	0.268	0.098
Calcium	-0.124	-0.081	-0.097	-0.034
Phosphorus	0.198	0.139	0.122	0.049
Hemoglobin	-0.256	-0.318	-0.397	-0.083

The correlation coefficients (r) in Table 2 represent the strength and direction of the relationship between mucocutaneous changes and laboratory markers. Positive values indicate a positive correlation, while negative values indicate a negative correlation.

- Xerosis showed a positive correlation with urea (r=0.312, p<0.001), creatinine (r=0.255, p=0.002), and CRP (r=0.187, p=0.032), suggesting that higher levels of these markers were associated with more severe xerosis.
- Pruritus exhibited a positive correlation with urea (r=0.244, p=0.007), creatinine (r=0.187, p=0.049), and CRP (r=0.326, p<0.001),

indicating that these laboratory markers were associated with increased pruritus severity.
- Pallor was negatively correlated with hemoglobin ($r=-0.397$, $p<0.001$), suggesting that lower hemoglobin levels were associated with more pronounced pallor.
- Uremic frost showed weak correlations with the laboratory markers, with none reaching statistical significance.

These preliminary findings indicate potential associations between certain laboratory parameters and the severity of mucocutaneous changes in ESRD patients. Further analysis and regression modeling are needed to explore these relationships in more detail, considering potential confounding factors.

DISCUSSION

The discussion section delves into the interpretation of our study's findings on mucocutaneous changes in end-stage renal disease (ESRD) patients undergoing regular hemodialysis. This section explores the implications of our results, their clinical relevance, and the potential mechanisms underlying these mucocutaneous manifestations.

Prevalence and Nature of Mucocutaneous Changes: Our study revealed a high prevalence of mucocutaneous changes among ESRD patients undergoing regular hemodialysis. The most common alterations included xerosis (45.6%), pruritus (32.1%), pallor (27.4%), and the relatively rare uremic frost (4.3%). These findings align with previous studies, emphasizing the significance of these mucocutaneous alterations in the ESRD population [1][2].

Xerosis and Pruritus: Xerosis, characterized by dry and scaly skin, was the most prevalent mucocutaneous change observed in our study. This condition, often associated with pruritus (itchiness), has a profound impact on the quality of life of ESRD patients. The high prevalence of xerosis and pruritus is consistent with existing literature [3].The relationship between xerosis and ESRD is complex. Uremia, characterized by elevated urea and creatinine levels, is believed to contribute to skin dryness in ESRD patients. Uremic toxins can disrupt skin barrier function and alter lipid composition, resulting in impaired epidermal hydration and increased transepidermal water loss [4][5]. Chronic inflammation, another hallmark of ESRD, may exacerbate xerosis by promoting proinflammatory cytokines that further disrupt skin integrity [6]. Pruritus, often co-occurring with xerosis, is a distressing symptom in ESRD patients. Our study found a positive correlation between pruritus severity and urea, creatinine, and C-reactive protein (CRP) levels. This suggests that both uremia and inflammation play roles in the development of pruritus in this population. The exact mechanisms underlying pruritus in ESRD remain incompletely understood but likely involve a complex interplay of neural sensitization, neurogenic inflammation, and peripheral neuropathy [7].

Pallor and Anemia: Pallor, characterized by skin and mucous membrane paleness, was observed in a substantial proportion (27.4%) of ESRD patients in our study. Pallor is a clinically relevant finding, often linked to underlying anemia, which is a common comorbidity in ESRD patients [8]. Our study identified a significant negative correlation between pallor and hemoglobin levels, indicating that lower hemoglobin levels were associated with more pronounced pallor. Anemia in ESRD is primarily attributed to reduced erythropoietin production by dysfunctional kidneys, leading to inadequate red blood cell production [9]. Anemia contributes to pallor by reducing the oxygen-carrying capacity of blood, resulting in tissue hypoxia and pale skin and mucous membranes. The management of anemia in ESRD often involves erythropoiesis-stimulating agents and iron supplementation to optimize hemoglobin levels and alleviate pallor [10]. Timely and appropriate management of anemia is essential not only for pallor but also for overall patient well-being, as anemia can lead to fatigue, reduced exercise tolerance, and cardiovascular complications.

Uremic Frost: Uremic frost, a relatively rare mucocutaneous manifestation, was observed in 4.3% of our study population. This striking clinical finding, characterized by crystalline deposits on the skin, serves as a visual reminder of the profound metabolic disturbances accompanying ESRD [11]. The exact pathogenesis of uremic frost remains unclear but is thought to involve the crystallization of urea and other solutes on the skin surface when perspiration evaporates, leaving behind crystalline residues [12]. The clinical significance of uremic frost lies in its potential association with severe uremia. Although uncommon, uremic frost may indicate advanced renal dysfunction and the need for prompt medical attention. Furthermore, addressing the underlying uremia is critical for managing this rare mucocutaneous presentation.

Comparative Literature: Our study's findings align with previous research highlighting the prevalence of mucocutaneous changes in ESRD patients. Xerosis and pruritus are commonly reported in the literature, with studies consistently implicating uremia and inflammation as key contributors [13]. Pallor, indicative of anemia, is a well-recognized complication in ESRD [14]. While uremic frost is rare, its presence underscores the severity of metabolic derangements in some ESRD patients [15]. The management of mucocutaneous changes in ESRD patients involves a multidisciplinary approach. Dermatological interventions, including emollients and topical corticosteroids for xerosis, and antipruritic therapies for pruritus, can provide symptomatic relief

[16]. Addressing underlying biochemical abnormalities, such as optimizing hemoglobin levels in anemia and managing uremia, is paramount for long-term improvement [17].

Limitations and Future Directions: Our study has several limitations. The cross-sectional design restricts our ability to establish causality between mucocutaneous changes and specific factors. Additionally, the single-center setting may limit the generalizability of our findings. Unmeasured variables and confounding factors could influence the study results.Future research in this area should consider prospective longitudinal studies to elucidate the temporal relationships between mucocutaneous changes and biochemical parameters. Investigating the impact of tailored interventions, such as optimizing anemia management and controlling uremia, on mucocutaneous outcomes may provide valuable insights into improving the quality of life for ESRD patients.

CONCLUSION

In conclusion, our study underscores the high prevalence of mucocutaneous changes in ESRD patients undergoing regular hemodialysis. These alterations, encompassing xerosis, pruritus, pallor, and uremic frost, significantly impact patients' quality of life and may serve as clinical indicators of underlying biochemical abnormalities. Recognizing the multifactorial nature of these mucocutaneous changes and their associations with uremia and inflammation is crucial for tailored patient care. Further research is needed to explore effective interventions and management strategies to mitigate these mucocutaneous manifestations and enhance the overall well-being of ESRD patients.

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