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Short Communication

Correlation of skin moisture and serum urea level with dermatology life quality index in patients with chronic kidney disease on hemodialysis: A cross-sectional study

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Abstract

Chronic kidney disease (CKD) is a global health concern, with a 10% global prevalence. Its prevalence may further increase in the coming decades, thereby increasing the risk of uremic xerosis. Approximately 50–90% of patients with CKD have xerosis, leading to pruritus that affects their quality of life due to sleep disturbances, anxiety, and depression. However, the exact mechanisms underlying xerosis in CKD remain unknown. The aim of this study was to assess the correlation of serum urea levels and skin moisture with quality of life in patients with CKD. This cross-sectional study was conducted at the Universitas Sumatera Utara Hospital from March to December 2023. Patients with CKD aged ≥18 years who were undergoing hemodialysis for at least 3 months were included in this study. A translated Dermatology Life Quality Index (DLQI) questionnaire was employed to assess the patient's quality of life. Serum urea levels and skin moisture were determined using venous blood and the Skin Moisture Checker MY-808S tool, respectively. In total, 67 patients with CKD, including 61.2% males and 32.8% individuals aged >60 years, were enrolled in this study. The mean age was 52.73±13.08 years. The mean serum urea levels, skin moisture, and DLQI scores were 154.08±49.10 mg/dL, 36.22±2.34%, and 4.67±3.98, respectively. No difference in DLQI scores was observed between normal and high serum urea levels or between dry and normal skin moisture levels (p=0.156 and p=0.804, respectively). Spearman's correlation analysis revealed no correlation between serum urea levels and average skin moisture with DLQI (p=0.600 and p=0.353, respectively), indicating that multiple factors contribute to the dermatological quality of life in patients with CKD. Notably, DLQI in patients with CKD can be simultaneously affected by multiple factors, such as diverse sociodemographic backgrounds, coping mechanisms, and the impact of symptoms associated with CKD, other than serum urea levels and average skin moisture. Therefore, adopting a multifactorial and individualized approach is crucial to improving the DLQI scores of patients with CKD.

Keywords: Chronic kidney disease, DLQI, serum urea, skin moisture, uremic xerosis

Introduction

Chronic kidney disease (CKD) is a significant global health concern affecting approximately 850 million people worldwide, with a prevalence rate of 10% [1]. The global prevalence of CKD increased by 33% between 1990–2017 and is expected to rise further in the coming decades due to the aging global population, increasing population growth, and the rising prevalence of

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contributing diseases such as diabetes and cardiovascular diseases [2,3]. The incidence of CKD is notably high in Indonesia, with a prevalence of 0.38% in 2018, indicating that 4 out of every 1000 people were diagnosed with CKD, and 19.3% of these patients underwent hemodialysis [4].

Based on Kidney Disease: Improving Global Outcomes (KDIGO), CKD is defined as abnormalities in renal structure with a declining glomerular filtration rate (GFR) below 60 mL/min/1.73 m^2 for more than three months, regardless of etiology [5]. Deteriorating kidney clearance results in the accumulation of serum creatinine, urea, and uric acid, causing metabolic imbalances and altering skin structure [6]. Approximately 50–100% of patients with end-stage renal disease (ERSD) develop at least one cutaneous manifestation, such as pruritus, xerosis, pigmentary changes, and ichthyosis [7]. These changes may affect the quality of life of the patients, contributing to sleep disturbances, anxiety, depression, aesthetic concerns, and lowered self-esteem [8], ultimately leading to a poorer overall quality of life. The Dermatology Life Quality Index (DLQI) is used to measure the quality of life related to skin problems [9] and is widely used to treat skin diseases across different populations. Designed for adults aged >18 years, the DLQI comprises simple questions that capture patients' perspectives in six domains: symptoms and feelings, daily activities, leisure, work and school, personal relationships, and treatment. This instrument enables the evaluation of new therapies, comparison of different healthcare delivery methods, and assessment of the impact of skin conditions on patients' lives [9,10].

Xerosis is one of the most common cutaneous manifestations in patients with CKD, occurring in approximately 50–90% of patients with ERSD. Up to 90% of patients with CKD still experience xerosis despite undergoing dialysis [11], and the exact mechanism underlying xerosis in patients with CKD remains unclear. Uremic xerosis is characterized by widespread rough and scaly skin with marked involvement of legs, hands, back, and chest [12]. Changes in skin anatomy in patients with CKD result in an impaired skin barrier, which is further exacerbated by increased susceptibility to irritation due to external stimuli, such as the sun, irritants, and low humidity, increasing the risk of uremic pruritus [13]. Therefore, it impacts the quality of life, morbidity rate, and burden cost in patients with CKD; however, it is still commonly underestimated in clinical practice [14]. Data regarding the impact of serum urea levels and skin moisture on the quality of life of patients with CKD are limited. The aim of this study was to evaluate the correlation of skin moisture and serum urea level with DLQI in patients with CKD undergoing hemodialysis.

Methods

Study settings and patients

This cross-sectional, observational, and analytical study involved patients with CKD undergoing hemodialysis at the Universitas Sumatera Utara Hospital, Medan, Indonesia. The minimum sample size of 47 respondents was calculated using a correlation coefficient analytical formula [15]. To ensure more accurate population representation, this study included an additional 20 respondents, resulting in 67 respondents. This addition aimed to minimize sampling errors, account for potential participant dropouts, and anticipate respondents who might provide consecutively straight 'yes' or 'no' responses on the DLQI. Samples were collected consecutively between March and December 2023. CKD was diagnosed by a nephrologist based on either increased markers of kidney damage (serum urea levels and creatinine), decreased GFR below 60 mL/min/1.73 m^2, or structural renal abnormalities detected through imaging for at least three months. The inclusion criteria were patients with CKD aged >18 years who underwent hemodialysis for at least three months. Patients with cutaneous diseases long before CKD diagnosis and those who regularly used moisturizers were excluded from the study. Patients who met the inclusion criteria and were willing to participate were recruited after signing the informed consent.

Data collection

Sociodemographic data such as sex, age, ethnicity, education, job, hemodialysis frequency, and duration were collected during the interviews and from medical records. Skin moisture on the forehead, outer corner of the eye, and inner forearm was analyzed using the Skin Moisture Checker MY-808S tool (Scalar Corporation, Tokyo, Japan). The Scalar Moisture Checker MY-

808S assesses skin moisture by measuring the dielectric capacitance of the stratum corneum (skin capacitance), displaying the percentage of hydration based on the correlation between water content and dielectric percentage [16]. The skin moisture levels were categorized into three groups: dry, normal, and moist. The cut-off points for these classifications were established using standard values from the Scalar Moisture Checker MY-808S (Scalar Corporation, Tokyo, Japan). Skin moisture was classified as dry, normal, and moist if it was <36%, 36–54%, and >54% for the forehead; <40%, 40–54%, and >54% for the outer corner of the eye; and <36%, 36–45%, and >45% for the inner forearm, respectively [17]. Serum urea levels were measured from patients' venous blood samples and classified according to cut-off points established by the normal value reference from Universitas Sumatera Utara Hospital's laboratory (low <10 mg/dL; normal 10–50 mg/dL; high >50 mg/dL). Patients were interviewed using the translated version of the DLQI questionnaire in the Indonesian language, which has been fully linguistically and statistically validated to determine the quality of life of individuals with various skin diseases [18]. A trained research assistant (a general practitioner) conducted all interviews, with authors excluded from this process to prevent bias.

Dermatology Life Quality Index (DLQI) questionnaire

The DLQI consisted of 10 questions that measure the severity of skin problems affecting a patient's life over the past week, covering six domains: symptoms and feelings, daily activities, leisure, work and school, personal relationships, and treatment. Each question was answered by selecting one option from five possible answers: "not relevant" (score 0), "not at all" (score 0), "a little" (score 1), "a lot" (score 2), or "very much" (score 3). The total score was obtained by summing all responses, which was further classified into five levels indicating the degree of impact on patients' lives as "no effect" (score 0–1), "small effect" (score 2–5), "moderate effect" (score 6–10), "very large effect" (score 11–20), and "extremely large effect" (score 21–30). The questionnaire yields a minimum score of 0 and a maximum score of 30; the higher the score, the poorer the dermatological quality of life [9].

Statistical analysis

The normality of all variables was assessed using the Kolmogorov-Smirnov test. The Mann-Whitney test was used to compare the mean DLQI scores between skin moisture and serum urea levels. Spearman's correlation coefficient was employed to determine the correlation between skin moisture and serum urea level with DLQI. Statistical significance was set at $p<0.05$ (two-sided). Partial correlation analysis was also performed to determine the direct correlation between the two variables of interest after controlling for the linear influence of third, fourth, or additional confounding variables by keeping the correlation values of confounding variables constant [19,20]. A variable was considered to exert an independent effect on the variable of interest if its partial correlation coefficient yielded a statistically significant p-value of <0.05. Conversely, a variable was considered non-independent if its partial correlation coefficient was not statistically significant. Serum urea levels and average skin moisture were alternatively controlled or designated as variables of interest in the partial correlation analysis. All statistical analyses were performed using IBM SPSS Statistics version 22 (IBM, New York, USA).

Results

Participant characteristics

Sixty-seven respondents were eligible for this study, and their characteristics are presented in **Table 1.** Most respondents were male (61.2%) and older than 60 years old (32.8%). The mean age of the respondents was 52.73±13.08 years. Serum urea levels of most patients were >50 mg/dL (95.5%), and only three patients had serum urea levels of 10–50 mg/dL (4.5%). The mean serum urea level was 154.08±49.10 mg/dL. Approximately 97% of the respondents underwent hemodialysis twice a week. The mean skin moisture on the forehead, corner of the eye, and inner forearm were 37.12±3.09%, 39.25±3.32%, and 31.99±3.03%, respectively, with an average skin moisture of 36.22±2.34%. Only 7.5% of respondents reported that xerosis had a very large effect on their lives. In contrast, 25.4%, 40.3%, and 26.9% of respondents reported no, small, and moderate impacts of xerosis on their lives, respectively.

Table 1. Characteristics of patients with chronic kidney disease undergoing hemodialysis (n=67)

Characteristics	Frequency (%)	Mean±SD	95%CI
Sex			
Male	41 (61.2)		
Female	26 (38.8)		
Age (years)		52.73±13.08	49.79–55.93
20–30	5 (7.5)		
31–40	10 (14.9)		
41–50	9 (13.4)		
51–60	21 (31.3)		
>60	22 (32.8)		
History of hemodialysis (years)		2.52±2.44	1.98–3.07
<2	27 (40.3)		
2–5	32 (47.8)		
6–10	7 (10.4)		
>10	1 (1.5)		
Hemodialysis frequency (per week)		2.00±0.17	1.96–2.04
1	1 (1.5)		
2	65 (97.0)		
≥3	1 (1.5)		
Serum urea level (mg/dL)		154.08±49.10	142.53–165.09
Low (<10)	0 (0)		
Normal (10–50)	3 (4.5)		
High (>50)	64 (95.5)		
Skin moisture on the forehead (%)		37.12±3.09	36.66–38.15
Dry (<36)	21 (31.3)		
Normal (36–54)	46 (68.7)		
Moist (>54)	0 (0)		
Skin moisture at the outer corner of the eye (%)		39.25±3.32	38.46–40.04
Dry (<40)	40 (59.7)		
Normal (40–54)	27 (40.3)		
Moist (>54)	0 (0)		
Skin moisture at the inner forearm (%)		31.99±3.03	31.23–32.70
Dry (<36)	61 (91.0)		
Normal (36–45)	5 (7.5)		
Moist (>45)	1 (1.5)		
Average skin moisture (%)		36.22±2.34	35.66–36.78
Dry (<37.3)	47 (70.1)		
Normal (37.3–51)	20 (29.9)		
Moist (>51)	0 (0)		
Dermatology Life Quality Index (DLQI) score (%)		4.67±3.98	3.75–5.63
No effect (score 0–1)	17 (25.4)		
Small effect (score 2–5)	27 (40.3)		
Moderate effect (score 5–10)	18 (26.9)		
Very large effect (score 11–20)	5 (7.5)		
Extremely large effect (score 21–30)	0 (0)		

The mean DLQI score in this study was 4.67±3.98 (95%CI: 3.75–5.63) (**Table 1**). No significant difference in the DLQI scores was observed between patients with normal and elevated serum urea levels (p=0.156) or between those with dry and normal skin moisture levels (p=0.804) (**Table 2**). Similarly, Spearman's correlation indicated no correlation between serum urea levels and average skin moisture with DLQI scores (p=0.600 and p=0.353, respectively) (**Table 3**).

Table 2. Mean Dermatology Life Quality Index (DLQI) score and its correlation with serum urea levels and skin moisture

Characteristics	DLQI score (mean±SD)	p-value [a]
DLQI score	4.67±3.98	
Serum urea level (mg/dL)		
Normal (10–50)	1.67±1.53	0.156
High (>50)	4.81±4.00	
Skin moisture on the forehead (%)		
Dry (<36)	4.90±4.50	0.924
Normal (36–54)	4.57±3.76	
Skin moisture at the outer corner of the eye (%)		
Dry (<40)	4.95±4.16	0.603
Normal (40–54)	4.26±3.74	

Characteristics	DLQI score (mean±SD)	*p*-value [a]
Skin moisture at the inner forearm (%)		
Dry (<36)	4.59±3.89	0.640
Normal (36–45)	5.00±5.57	
Average skin moisture (%)		
Dry (<37.3)	4.62±3.69	0.804
Normal (37.3–51)	4.80±4.69	

[a] Analyzed using Mann-Whitney test

A partial correlation test was used to examine the linear association between serum urea levels and DLQI while controlling for skin moisture. No significant partial correlation was observed between serum urea levels and DLQI after controlling for skin moisture ($r_{partial}$=-0.020; p=0.874) (**Table 4**). The negative direction suggested that higher serum urea levels were associated with lower DLQI scores. However, when comparing this with the zero-order correlation (r=-0.065; p=0.600), controlling for skin moisture decreased the correlation strength and significance between serum urea levels and DLQI (**Table 3**).

Furthermore, the partial correlation between skin moisture levels and the DLQI was assessed while controlling for serum urea levels. No significant partial correlation was observed between skin moisture levels and DLQI ($r_{partial}$=-0.093; p=0.460) (**Table 4**). The negative direction suggested that higher skin moisture levels were associated with lower DLQI scores. Interestingly, when compared to the zero-order correlation (r=-0.115; p=0.353), controlling for serum urea levels decreased the correlation strength and significance between these two variables (**Table 3**).

Table 3. Correlation among serum urea levels, skin moisture, and Dermatology Life Quality Index (DLQI) score

Variables	Serum urea level		Average skin moisture		DLQI score	
	Spearman's rho	*p*-value	Spearman's rho	*p*-value	Spearman's rho	*p*-value
Serum urea level	1	-	-0.047	0.703	-0.065	0.600
Average skin moisture	-0.047	0.703	1	-	-0.115	0.353
DLQI	-0.065	0.600	-0.115	0.353	1	-

Table 4. Partial correlation analysis between serum urea levels and skin moisture and Dermatology Life Quality Index (DLQI)

Independent variable	DLQI	
	Partial correlation coefficient (*r*)	*p*-value
Serum urea level	-0.020 [a]	0.874 [a]
Average skin moisture	-0.093 [b]	0.460 [b]

[a]After controlling for average skin moisture
[b]After controlling for serum urea level

Discussion

The present study evaluated the correlation of serum urea levels and skin moisture with the DLQI score in patients with CKD. CKD was predominantly observed in males, who comprised 61.2% of the total participants. The highest number of individuals with CKD were aged >60 years (32.8%), and the mean age was 52.73±13.08 years. These results are consistent with those reported in previous studies conducted in Indonesia [21-23]. However, studies from other countries have reported contradictory results with a higher prevalence in females [24,25]. The reason underlying these contradictory results is yet to be determined and is probably complex [26]. In most studies, CKD has been predominantly reported in patients aged >50 years [21-23], and its prevalence may increase exponentially with increasing age as older people are more vulnerable to aging diseases such as diabetes and cardiovascular diseases, leading to a higher risk of CKD [27]. The mean DLQI score in this study was 4.67±3.98, with a median of 4. This result is consistent with that of other studies, with median DLQI scores ranging from 2 to 3 [28,29].

The results of this study indicated no significant correlation between serum urea levels and DLQI scores. Furthermore, a negative correlation was observed, although the underlying cause of this negative correlation remains unclear. To date, no study has specifically examined the

relationship between serum urea levels and DLQI scores. Pruritus could be a contributing factor influencing DLQI scores. Notably, no significant differences in blood urea nitrogen levels have been reported between patients with CKD with and without pruritus [30,31]. Pruritus occurs in 22–90% of patients with CKD [6] and may involve multiple factors, although its precise mechanism is poorly understood. It has been hypothesized that pruritus may occur due to the accumulation of pruritogens, including uremic toxins, histamines, prostaglandins, neuropeptides, proteases, and proinflammatory cytokines, in cutaneous tissue [21]. In patients with CKD, immune dysregulation, as evidenced by elevated inflammatory markers such as T cells, interleukins, mast cells, histamine, and C-reactive protein, leads to microinflammation, ultimately sensitizing the end nerve fibers in the skin that transmit itching sensations to the brain [22,23]. Additionally, susceptibility to these sensitized nerve fibers may be exacerbated by peripheral neuropathy, which is commonly observed in patients with pruritus undergoing dialysis [24,25].

An association between pruritus and xerosis may contribute to increased DLQI scores. Moderate to severe xerosis is linked to a 50–100% increase in uremic pruritus cases [14]. The incidence of xerosis among patients with CKD is 50–85%, with 30–40%, 35–50%, and 15–30% experiencing mild, moderate, and severe xerosis, respectively [12]. Structural alterations in the skin of patients with CKD, such as reduced sweat production, dermal elastin fragmentation, impaired skin perfusion, and a diminished number and size of sebaceous glands and sweat glands, cause skin dehydration due to decreased sweat and sebum excretion [11]. Furthermore, increased surface pH may activate proteases, such as tryptase and chymase, resulting in stratum corneum desquamation and skin barrier impairment [12]. Additionally, the fluid shift during dialysis can exacerbate xerosis by depleting moisture from the dermis of patients with CKD patients [11].

In this study, no significant correlation between skin moisture levels and DLQI score was observed. However, the negative direction of the relationship indicated that higher skin moisture may be associated with a lower DLQI score and vice versa. Nevertheless, skin moisture may not be the only factor affecting the DLQI in patients with CKD. Notably, other studies have also reported opposite results [12,14,29,32,33]. A survey by Szepietowski *et al.* revealed significantly higher mean DLQI and 12-Item Short-Form Health Survey (SF-12) scores in patients with CKD and xerosis than in the average population [12]. Other studies have also reported a weak to strong significant correlation between xerosis cutis and the quality of life in patients with CKD [14,29,32]. Xerosis can indirectly affect the patient's quality of life by inducing pruritus [14,31]. Patients with CKD and pruritus on dialysis had significantly reduced stratum corneum hydration and transepidermal water loss compared with non-pruritic patients. Impaired barrier function, which causes increased transepidermal water loss, can lead to skin dryness and itching [34]. Increased xerosis severity also increases pruritus frequency, resulting in a higher DLQI score [35].

The correlation among serum urea levels, skin moisture, and the DLQI may be influenced by other confounding factors. To test this, a partial correlation analysis was conducted to examine the correlation between serum urea levels and DLQI, while controlling for skin moisture as a confounding factor. The results revealed a greater extent of negative direction for this relationship (**Table 4**), indicating that controlling for skin moisture increased the correlation strength between serum urea levels and DLQI. Furthermore, the partial correlation between skin moisture and DLQI was also analyzed, controlling for serum urea level as the confounding factor. The results yielded a lesser extent of negative direction for this relationship (**Table 4**), indicating that controlling for serum urea levels decreased the correlation strength between skin moisture and DLQI. Collectively, these results suggest that rather than being directly associated with the DLQI, factors such as serum urea levels and skin moisture may interact with other variables that influence an individual's quality of life, warranting further studies to identify other factors. Furthermore, the correlation between serum urea levels and skin moisture in this study also showed a correlation in a negative direction (r=-0.047), indicating that higher serum urea levels are associated with lower skin moisture and vice versa. This suggests that serum urea levels do not directly impact DLQI but indirectly decrease DLQI by lowering skin moisture.

The lack of correlation between serum urea level and skin moisture with the DLQI in patients with CKD may be attributed to the multifaceted nature of the DLQI, the complexity and variability

of CKD symptoms, different sociodemographic backgrounds of the patients, and potential measurement limitations [36,37]. Skin moisture does not effectively reflect the overall dermatological health and may not significantly impact the broader aspects of the DLQI. Patients with CKD often experience a wide range of symptoms and complications due to CKD, including fatigue, pain, and psychological stress, in addition to its dermatological manifestations, all of which may have a more substantial impact on quality of life than uremic xerosis. Therefore, dermatological manifestations may not be prioritized [38]. Patient recovery may also be affected by lowering DLQI scores. As in our study, most patients receive motivation from fellow patients and healthcare workers about their diseases, often forming support groups. This support helps patients better understand and accept their current health status. [39,40]. Regarding sex differences, female patients may report xerosis more frequently than male patients, as women often find skin dryness to be more distressing. Notably, female patients had higher mean DLQI scores than male patients in this study (5.19±4.02 and 4.34±3.97, respectively). Similar results were also reported by Szepietowski *et al.* [14]. Patient characteristics should be controlled to assess the correlation accurately and minimize measurement limitations. Lastly, skin moisture and serum urea levels might be indirectly associated with DLQI. Szepietowski *et al.*, through a partial correlation analysis, reported that xerosis itself does not directly impact DLQI but further lowers patients' quality of life by exacerbating pruritus [14].

This study confirmed that no correlation occurs among serum urea, skin moisture, and DLQI. However, patients with CKD still develop dermatological manifestations that further affect their DLQI. Therefore, other factors associated with DLQI should be identified and analyzed to explore the potential roles of serum urea and skin moisture as indirect contributors to DLQI. DLQI scores in patients with CKD should be improved by employing multifaceted approaches, not only by treating renal dysfunction but also by managing dermatological manifestations. Xerosis and early pruritus in patients with CKD can be treated with daily moisturizing emollients. Alternatively, patients with CKD and persistent pruritus can be treated with antihistamines or gabapentinoid derivatives. Other treatments currently in clinical trials also include pruritus treatment options such as difelikefalin, nalbuphine, and nalfurafine [41]. Additionally, providing psychological support to address the psychosocial effects is essential, thereby necessitating a multidisciplinary approach involving nephrologists, dermatologists, and psychiatrists [42,43].

This study also has some limitations. First, the small sample size in our study does not fully represent the Indonesian population, particularly in rural regions, because our study was conducted at a secondary hospital located in an urban area. Second, the "not relevant" answer choice on the DLQI questionnaire might contribute to a false-negative answer, potentially leading to an underestimation of the effect, as 1.49% of the total responses were "not relevant."

Conclusion

This study found that serum urea and skin moisture levels were not significantly correlated with the DLQI scores in patients with CKD, indicating multiple factors influence the dermatological quality of life in these patients. Consequently, holistic management is necessary to manage dermatological complaints in these patients and improve their quality of life.

Ethics approval

This study was approved by the Ethical Committee of Universitas Sumatera Utara, Medan, Indonesia, on May 03, 2023 (Approval No. 399/KEPK/USU/2023).

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Competing interests

The authors declare that there are no conflicts of interest.

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Underlying data

Calculation of sample size is available at: https://doi.org/10.6084/m9.figshare.26339029.

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