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Association Between Uremic Pruritus and Differential Leukocyte Counts Among Hemodialysis Patients in Ibn Sina Dialysis Center

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Abstract

Background: Pruritus is a common and bothersome symptom of chronic kidney disease (CKD). According to the most recent epidemiologic data, about 40% of patients with end-stage renal disease (ESRD) experience moderate to severe pruritus. The reason for uremic pruritus remains poorly understood, but recent studies suggest a strong association with the inflammatory process and elevated white blood cell (WBCs).

Objectives: This study aims to investigate the correlation between uremic pruritus (UP) and differential leukocyte levels in patients with CKD undergoing dialysis (Hemodialysis patients), and to examine the potential role of inflammation in the severity of pruritus.

Patients and Methods: A study was conducted at Ibn Sina Dialysis Center, Diyala Governorate, Iraq. The study involved 150 hemodialysis (HD) patients, divided into two groups: 75 patients with UP and 75 without UP. The control group consisted of 26 healthy individuals. Out of 226 HD patients at the Dialysis Center, those under 20 years old, as well as patients with hepatitis C or hepatitis B, were excluded. From each patient and control in this study, 3 ml of venous blood was collected before dialysis, placed in an ethylene diamine tetraacetic acid (EDTA) tube for leukocyte differential count, and analyzed at the educational laboratory of Baqubah Teaching Hospital.

Results: The results showed that 33.8% of HD patients had uremic pruritus and had a significantly higher eosinophil level when compared with patients without UP and controls. While basophil and neutrophil showed no significant difference in patients with UP and without UP when compared with the control. When compared to patients without UP, HD patients with UP had higher lymphocyte counts; however, there was no discernible difference between the control group, hemodialysis patients with UP, and patients without UP.

Conclusion: It was shown that eosinophils may play an essential role in the pathogenesis of UP by inducing and secreting materials that exacerbate its severity. Lymphocytes can also play a role in the pathogenesis of UP by secreting cytokines.

Keywords: Uremic pruritus, Leukocytes, Hemodialysis, Diyala, Eosinophil.

Introduction

Uremic pruritus is a common, unpleasant symptom of CKD, and it's linked to a lower quality of life and bad outcomes. It's now widely acknowledged as a major research priority (1). Chargin and Keil

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first reported on uremic pruritus in 1932 (2). It occurs as a frequent or near-daily incidence of itch that spans large bilaterally symmetrical surface areas (3). It is an unpleasant sensation that has been recognized as a frequent complication in patients with chronic kidney disease (4,5). One of the most common and burdensome dermatological symptoms affecting patients undergoing dialysis is CKD-associated pruritus (CKD-aP) (6). Skin pruritus can affect any part of the body and last for various durations, resulting in secondary scratches. Nodular prurigo, for example, is a moss-like skin condition that has a significant impact on the patient's physical and mental health (7). It affects more than one-third of dialysis patients and has an incidence of 15% to 49% (5). Thirty percent to sixty percent of patients in this group had symptoms for more than a year (8). As CKD progresses and the incidence of pruritus increases, the patient's quality of life deteriorates. According to some studies, uremic pruritus is linked to a greater risk of mortality in patients with chronic kidney disease (9). CKD was recognized as a cause of immune dysfunction that arises from a combination of factors, including uremia, malnutrition, chronic inflammation, and mineral bone disease (10). The toxic metabolic wastes accumulate in uremic states, promoting cytokine accumulation and persistent systemic inflammation, which causes acquired immune suppression due to the depletion of immune cells from low-grade persistent inflammation (11). The immune dysfunction is a risk factor for progression and mortality of CKD (12). Since a high total white blood cell (WBC) count often indicates inflammation and a low lymphocyte count indicates immune suppression, a high WBC count and a low lymphocyte count in patients with CKD are associated with a worse prognosis (13,14).

Another study has highlighted the immunological mechanisms contributing to uremic pruritus, indicating that it is closely related to systemic immune dysregulation and not merely a dermatologic or neurological condition. Patients on hemodialysis who experience pruritus have been found to have elevated white blood cell (WBC) counts, specifically eosinophils, basophils, and neutrophils. This suggests an inflammatory state that could play a role in the pathophysiology of the uremic pruritus (15). The interaction between uremic toxins and immune cells leads to chronic immune activation, promoting pruritogenic signaling (16). These findings suggest a possible inflammatory or immunological role in the pathogenesis of uremic pruritus, and understanding these immunological contributors is essential for developing targeted therapies (17).

Patients and Methods

Study design: This study was conducted on HD patients to assess the levels of different leukocytes in those with uremic pruritus. It took place at Ibn Sina Dialysis Center in Diyala, Iraq. During this period, the center had 226 patients. Patients under 20 years old, as well as those with hepatitis C and hepatitis B, were excluded, resulting in a study group of 150 patients (75 with UP and 75 without UP).

Questionnaire: A questionnaire was prepared, distributed, and collected from each patient and control group. Patients answered the questions in the Dialysis Center. For each case of uremic pruritus, a questionnaire was used to gather demographic information about age, sex, duration of dialysis, number of dialysis sessions per week, number of hours per dialysis session per day, and the severity of uremic pruritus.

Visual analyze scale: A VAS was used, which is a technique for converting non-numeric values into numeric values. It is a 10-point scale, with 0 indicating no pruritus and 10 indicating severe pruritus. One-centimeter intervals differentiate the numerical values. The categorization by Reich et al. was used as a reference when

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classifying the VAS score. They classified the severity of pruritus as follows: < 4 points was considered mild; ≥ 4 points but < 7 points was moderate; ≥ 7 points but < 9 points was severe; and ≥ 9 points was very severe pruritus (18).

Sample preparation and storage: All patients were examined by a dermatologist referred from Ibn Sina Dialysis Center. From each patient and control in this study, 3 ml of venous blood was collected before dialysis under complete aseptic conditions and put in an ethylene diamine tetraacetic (EDTA) tube (to prevent coagulation) for leukocyte differential. We utilized the DxH 520 Hematology Analyzer to measure white blood cell (WBC) counts in whole blood samples. The reference range for WBC counts in this analysis was established between 4,000 and 11,000 cells per microliter. **Differential leukocytes were recorded:** eosinophils, basophils, neutrophils, and lymphocytes. These measurements are performed in educational Laboratories in Baqubah Teaching Hospital.

Statistical Analysis

The data processing software package is used (SPSS, 2020) for Windows. Data are expressed as mean ± standard error (M ± SE). Differences between the means of the two major groups are analyzed using a t-test, and significance is tested at a two-tailed P-value. However, differences among subgroups are analyzed using one-way analysis of variance (ANOVA). If a significant difference is found, it is further analyzed using the least significant difference test (LSD). The P-value of differences <0.05 is considered significant. The Pearson correlation (R) accounted for the type and strength of the relationship between variables.

Results

Characterization of patients with pruritus under hemodialysis session: Table 1 shows the demographic and clinical characteristics of 75 patients undergoing hemodialysis with uremic pruritus. The age of the participants ranged from 20 to 70 years. Regarding the duration of hemodialysis, a higher proportion of patients (56%) had been on dialysis for more than 6 months, while 44% had been receiving treatment for less than 6 months. The data also show a male predominance among the pruritus cases, with 60% of patients being male and 40% female. In terms of itch distribution, 65.3% of patients reported localized pruritus, whereas 34.6% experienced generalized itching. Concerning the severity of itch, most patients (56%) reported moderate pruritus, followed by severe itching in 26.6%, and mild symptoms in 17.3% of the cases. The table also outlines the main risk factors associated with chronic kidney disease (CKD) in these patients. Hypertension was the most commonly reported risk factor (32%), followed by diabetic mellitus (17.3%) and kidney stones (17.3%). Chronic glomerulonephritis accounted for 12%, interstitial nephritis and unknown causes each for 8%, and polycystic kidney disease was identified in 5.3% of the cases. This data provides an overview of the key demographic, clinical, and etiological features of uremic pruritus in hemodialysis patients.

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Table 1. Characterization of uremic pruritus patients under hemodialysis treatments.

Age (year)	Range (20-70)		
Duration of Hemodialysis	More than 6 months	N= 42	
	Less than 6 months	N= 33	
Sex	Men	N= 45	(60 %)
	Women	N= 30	(40 %)
Type of itch	Localize	N= 49	(65.3 %)
	Generalize	N= 26	(34.6 %)
Severity of itch	Mild	N= 13	(17.3 %)
	Moderate	N= 42	(56 %)
	Sever	N= 20	(26.6 %)
Risk factor of CKD	Hypertension	N= 24	(32 %)
	Diabetic Mulitas	N= 13	(17.3 %)
	Kidney Stone	N=13	(17.3 %)
	Chronic Glomerulonephritis	N= 9	(12 %)
	Interstitial Nephritis	N= 6	(8 %)
	Polycystic Kidney Disease	N= 4	(5.3 %)
	Unknown	N= 6	(8 %)
Characteristics of Patients with Pruritus under hemodialysis treatments N = 75			

Differential leukocytes among patients with uremic pruritus and without uremic pruritus: Eosinophils increased significantly in hemodialysis patients with uremic pruritus (0.24 ± 0.02 x 10^9 /L) when compared with control (0.14 ± 0.02 x 10^9) (p-value= 0.010), and patients without uremic pruritus (0.09 ± 0.00 x 10^9 /L) (p-value= 0.000), but the results showed no any significant differences between hemodialysis patients without uremic pruritus and control group (p-value= 0.137).

Basophils and neutrophils cells showed a significant increase in hemodialysis patients with pruritus (0.04 ± 0.00 x 10^9 /L, and 4.29 ± 0.17 x 10^9 /L, respectively) (p-value= 0.000 and 0.001, respectively) and patients without pruritus (0.04 ± 0.00 x 10^9 /L, and 4.29 ± 0.17 x 10^9 /L, respectively) (p-value= 0.000 and 0.005, respectively) when compare with control (0.02 ± 0.00 x 10^9 /L, and 3.17 ± 0.19 x 10^9 /L, respectively). At the same time, it did not show any significant differences between hemodialysis patients with and without uremic pruritus (p-value= 0.051 and 0.376).

Lymphocytes increased significantly in hemodialysis patients with uremic pruritus (1.77 ± 0.06 x 10^9 /L) when compared with patients without uremic pruritus (1.60 ± 0.04 x 10^9) (p-value 0.002). The results showed non-significant differences between hemodialysis patients with uremic pruritus and the control group (p-value = 0.094) and patients without uremic pruritus and the control group (p-value = 0.938) (Table 2).

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Table 2. Differential leukocytes among patients with uremic pruritus, without uremic pruritus, and controls.

Groups	Eosinophils x10^9 /L (Mean ± SE)	Basophils x10^9 /L (Mean ± SE)	Neutrophils x10^9 /L (Mean ± SE)	Lymphocytes x10^9 /L (Mean ± SE)
Patients with uremic Pruritus (N=75)	0.24 ± 0.02	0.04 ± 0.00	4.54 ± 0.24	1.77 ± 0.06
Patients Without Uremic Pruritus (N=75)	0.09 ± 0.00	0.04 ± 0.00	4.29 ± 0.17	1.60 ± 0.04
Control (N=26)	0.14 ± 0.02	0.02 ± 0.00	3.17 ± 0.19	1.59 ± 0.08
P-value*	P vs W, P= 0.000 C vs P, p= 0.010 C vs W, P= 0.137	P vs W, P= 0.051 C vs P, p= 0.000 C vs W, P= 0.000	P vs W, P= 0.376 C vs P, p= 0.001 C vs W, P=0.005	P vs W, P= 0.002 C vs P, p= 0.094 C vs W, P= 0.938
P value <0.05, SE: standard error, C: control, P: pruritus, and W.P: without pruritus.				

Differential leukocytes among mild, moderate, and severe itch groups: Eosinophils showed no significant difference among patients with mild, moderate, and severe itch (0.28 ± 0.07, 0.20 ± 0.02, and 0.29 ± 0.06, respectively), with p-values of 0.341, 0.901, and 0.181, respectively. Additionally, basophils showed non-significant differences among patients with mild, moderate, and severe itch (0.04 ± 0.00, 0.04 ± 0.00, and 0.04 ± 0.02, respectively), with p-values of 0.351, 0.639, and 0.634, respectively. Neutrophils showed no significant difference among patients with mild, moderate, and severe itch (4.36 ± 0.48, 4.78 ± 0.35, and 4.13 ± 0.42, respectively), with p-values of 0.530, 0.762, and 0.261, respectively. Lymphocytes showed no significant differences among patients with mild, moderate, and severe itch (1.68 ±0.12, 1.79 ± 0.88, and 1.92 ± 0.15, respectively), with p-values 0.551, 0.253, and 0.421, respectively (Table 3).

Table 3. Leukocytes and differential among mild, moderate, and severe itch groups.

Groups	Basophils x10^9 /L (Mean ± SE)	Neutrophils x10^9 /L (Mean ± SE)	Eosinophils x10^9 /L (Mean ± SE)	Lymphocytes x10^9 /L (Mean ± SE)
Patients with mild itch (N=13)	0.04 ± 0.00	4.36 ± 0.48	0.28 ± 0.07	1.68 ± 0.12
Patients with moderate itch (N=42)	0.04 ± 0.00	4.78 ± 0.35	0.20 ± 0.02	1.79 ± 0.88
Patients with severe (N=20)	0.04 ± 0.02	4.13 ± 0.42	0.29 ± 0.06	1.92 ± 0.15
P-value*	MI vs MO, p= 0.351 MI vs S, p= 0.639 MO vs S, p= 0.634	MI vs MO, p= 0.530 MI vs S, p= 0.762 MO vs S, p= 0.261	MI vs MO, p= 0.314 MI vs S, p= 0.901 MO vs S, p= 0.181	MI vs MO, p= 0.551 MI vs S, p= 0.253 MO vs S, p= 0.421
P value <0.05, MI mild, MO moderate, and S severe.				

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Discussion

In this study, eosinophils increased significantly in hemodialysis patients with uremic pruritus compared to the control group and patients without uremic pruritus. However, there were no significant differences between hemodialysis patients without uremic pruritus and the control group. According to another study, an increase in eosinophils caused by various conditions facilitates the recruitment of type 2 helper T (Th2) cells and cytokine-induced activation of eosinophils, resulting in the release of these molecules and subsequent effects on the affected tissues (19). Kojima et al demonstrated that an allergic reaction to HD-related materials may have induced eosinophilia, and the resultant increase in eosinophils might cause allergic symptoms such as itching (20). Keithi-Reddy et al described a case of uremic pruritus in which the eosinophil count in the peripheral blood was 24 percent and the skin biopsy revealed eosinophil infiltration. The authors stated that the uremic condition most likely caused the eosinophilia, and that histamine release was involved in the pathogenesis (21). In another study, it was reported that eosinophil levels increase in patients who suffer from pruritus. The increase in eosinophils is standard in Hemodialysis patients and is mainly induced by allergy to material of the dialysis circuit (22). In this study, Basophils and neutrophil cells showed a significant increase in hemodialysis patients with pruritus, as well as in those without pruritus, compared to controls. However, there were no significant differences between hemodialysis patients with and without uremic pruritus. A study by Pisonin et al also showed that no significant relationship was seen between neutrophil counts or neutrophil percentage and pruritus (23). This study agrees with the results obtained by Diehn and Tefferi, who found no significant correlation between pruritus and basophil count (24). In this study, lymphocytes increased significantly in hemodialysis patients with UP compared to those without UP. However, the results showed no significant differences between hemodialysis patients with uremic pruritus and the control group, nor between patients without uremic pruritus and the control group. The alterations in host immune response have primarily been studied in ESRD patients. The function of lymphocytes, monocytes, and polymorphonuclear white blood cells is altered, resulting in an impaired host response to infection (25). In a study by Alshafei and Nour, it was shown that the total number of lymphocytes significantly decreased in patients with pruritus compared to control patients (those without uremic pruritus under hemodialysis) (26). The same result was found in a study by Litjens et al, which suggested that patients with CKD suffer from inflammation and low levels of lymphocytes (27). The result was also supported by a study by Ommen et al, who found that lymphopenia in ESRD patients (28). Vaziri indicates that the accumulation of uremic toxins could lower the number of T-lymphocytes (29). In Turkey, a study by Ozen et al found that a WBC count was a risk factor for UP development in HD patients, with elevated WBC levels (30). A previous study showed that inflammation and pro-inflammatory factors are essential in the development of UP (31). Ghassan et al indicate that there is no significant difference in WBC count was found in the patients who had no pruritus compared with patients with mild, moderate and severe pruritus (32), similar to the results of a study to Chiu et al which found there was no significant difference in WBC count between patients with uremic pruritus and patients without pruritus (33). In a recent study, Rowee and Yosipovitch found that Cutaneous T-cell lymphoma may cause unmanageable pruritus and may have the cytokine interleukin 31 as a mediator of itching (34). In this

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study, eosinophils showed no significant differences among patients with mild, moderate, and severe itching. Also, basophils, neutrophils, and lymphocytes showed no significant differences among patients with mild, moderate, and severe itching. A study in Baghdad by Ghassan et al found that there is no significant correlation between the severity of pruritus in pruritic patients and both WBC and neutrophil counts (32). This may be attributed to the fact that WBC and neutrophil counts were within the normal range in most patients involved in the study. Higher eosinophil levels are linked to more severe pruritus and a lower quality of life, according to a strong association between the absolute eosinophil count (AEC) and the Dermatology Life Quality Index (DLQI). Eosinophils are implicated in pruritic dermatoses (35).

Conclusion:

Uremic pruritus is a complex condition influenced by multiple factors, including inflammation and WBC counts. The result showed that eosinophils may play an important role in the pathogenesis of uremic pruritus by inducing and secreting materials that increase the severity of UP. Lymphocytes can also play a role in the pathogenesis of UP by secreting and inducing cytokines that cause UP. Further research is needed to explain the mechanisms and develop effective treatments.

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Ethical clearance: The patients and control participants completed the questionnaire in the study and provided a blood sample. The Ethical Approval Committee at the College of Medicine, University of Diyala, approved this study (Code no. 2025HMJ900).

Conflict of interest: None.

Use of Artificial Intelligence: The authors declare that they did not use generative artificial intelligence for the creation or preparation of this manuscript.

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العلاقة بين الحكة البولية وعدد كريات الدم البيضاء التفاضلي لدى مرضى غسيل الكلى في مركز ابن سينا لغسيل الكلى

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الملخص

الخلفية: : الحكة الجلدية عرض شائع ومزعج لمرض الكلى المزمن. ووفقًا لأحدث البيانات الوبائية، يعاني حوالي ٤٠٪ من مرضى الفشل الكلوي في مرحلته النهائية من حكة جلدية تتراوح بين المتوسطة والشديدة. لا يزال سبب الحكة الجلدية اليوريمية غير مفهوم جيدًا، لكن الدراسات الحديثة تشير إلى ارتباطها القوي بالعملية الالتهابية وارتفاع عدد خلايا الدم البيضاء.

الأهداف: تهدف هذه الدراسة إلى دراسة العلاقة بين الحكة اليوريمية (**UP**) ومستويات الكريات البيضاء التفاضلية في المرضى الذين يعانون من مرض الكلى المزمن الذين يخضعون لغسيل الكلى (مرضى غسيل الكلى)، وفحص الدور المحتمل للالتهاب في شدة الحكة.

المواد والطرق: أُجريت دراسة في مركز ابن سينا لغسيل الكلى، محافظة ديالى، العراق. شملت الدراسة ١٥٠ مريضًا يخضعون لغسيل الكلى، مُقسَّمين إلى مجموعتين: ٧٥ مريضًا مصابًا بالتهاب الكلى المزمن (**UP**) و٧٥ مريضًا غير مصاب به. تألفت المجموعة الضابطة من ٢٦ فردًا سليمًا. من بين ٢٢٦ مريضًا يخضعون لغسيل الكلى في مركز غسيل الكلى، استُبعد من تقل أعمارهم عن ٢٠ عامًا، بالإضافة إلى مرضى التهاب الكبد الوبائي (**C**) أو التهاب الكبد الوبائي (**B**). من كل مريض ومجموعة ضابطة في هذه الدراسة، جُمِع ٣ مل من الدم الوريدي قبل غسيل الكلى، ووُضِع في أنبوب حمض إيثيلين دياميين رباعي الأسيتيك (**EDTA**) لعد كريات الدم البيضاء التفاضلي، وحُلِّل في المختبر التعليمي بمستشفى بعقوبة التعليمي.

النتائج: أظهرت النتائج أن ٣٣,٨٪ من مرضى غسيل الكلى يعانون من حكة بولية، وأن مستوى الخلايا الحمضية لديهم أعلى بشكل ملحوظ مقارنةً بالمرضى غير المصابين بالتهاب الكلى المزمن ومجموعة الضبط. بينما لم يُظهر مستوى الخلايا القاعدية والعدلات فرقًا كبيرًا بين المرضى المصابين بالتهاب الكلى المزمن والمجموعة الضابطة. بالمقارنة مع المرضى غير المصابين بالتهاب الكلى المزمن، كان لدى مرضى غسيل الكلى المصابين بالتهاب الكلى المزمن عدد أعلى من الخلايا الليمفاوية؛ ومع ذلك، لم يكن هناك فرق ملحوظ بين المجموعة الضابطة، ومرضى غسيل الكلى المصابين بالتهاب الكلى المزمن، والمرضى غير المصابين بالتهاب الكلى المزمن.

الاستنتاج: وقد تبين أن الخلايا الحمضية قد تلعب دورًا أساسيًا في التسبب بالتهاب البنكرياس المزمن، وذلك من خلال تحفيز وإفراز مواد تُفاقم شدته. كما يمكن للخلايا الليمفاوية أن تلعب دورًا في التسبب بالتهاب البنكرياس المزمن من خلال إفراز السيتوكينات.

الكلمات المفتاحية: حكة بولية، كريات الدم البيضاء، غسيل الكلى، ديالا، الحمضات.

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