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Original Article

A Study of the Prevalence of Pruritus in Hemodialysis Patients and its Relationship with Laboratory Indicators and Dialysis Characteristics

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Abstract *- Pruritus is a common and frustrating problem in hemodialysis patients, causing discomfort and skin damage. Pathogenesis is still unknown, and it is thought to be multifactorial. The main goal of this study is to know the prevalence of pruritus in hemodialysis patients. 200 hemodialysis patients were included in this study. Data were collected using the Visual Analog Scale (VAS) questionnaire. We investigated whether the duration of hemodialysis, type of dialysate, Kt/V, and laboratory indicators such as phosphorous, calcium, magnesium, and blood urea were correlated to pruritus. Pruritus was found in 72.5% of the hemodialysis patients. 58% of the research samples studied were males, and 42% were females. There were no statistically significant differences between genders, the diseases leading to chronic kidney and the severity of itching. There are statistically significant differences between age groups, calcium and vitamin D intake, the type of hemodialysis device, the years of dialysis treatment, the type of anticoagulant, Kt/V, and the increase in the severity of itching(P<0.005). Pruritus remains an important and frustrating problem in dialysis patients. High levels of phosphorous, calcium, and urea contribute to itching.*

Keywords *- CKD, Hemodialysis, Pruritus, Itching, Uremic.*

1. Introduction

Chronic Kidney Disease (CKD) is kidney function impairment that lasts longer than three months and is characterized by structural or functional problems with the kidney. Some individuals experience chronic kidney insufficiency, which is indicated by a decline in glomerular filtration rate [1], and this condition may progress to a fatal form of chronic kidney disease [2,3].

End Stage Renal Disease (ESRD) is the fifth stage of chronic renal failure, where hemodialysis, peritoneal dialysis, or a kidney transplant is required [4]. The glomerular filtration rate is less than 15 ml/min at this stage.

Chafing and scratching are uncomfortable symptoms of pruritus. Patients continue to struggle with the frustrating issue of pruritus, which damages their skin and causes discomfort. It frequently results in sleep difficulties, sadness, anxiety, and a reduced quality of life [5, 6].

Uremic Pruritus (UP) is a common name for itching. It has been argued that the phrase "CKD-associated pruritus" is more precise because there is no actual cause-and-effect relationship between uremia and pruritus and because pruritus is typically not observed in patients with acute kidney disease [7,8].

The prevalence of pruritus in hemodialysis patients ranged between 50% to 90%, as reviewed in medical literature. It has been assumed that the pruritus seen in dialysis patients is uremic if no other cause exists. Before we say that uremic pruritus is the cause, we must rule out other causes, such as cholestasis and hypersensitivity reactions. The pathophysiology of pruritus is not well understood, and the exact cause of it in patients with CKD is unknown, as many factors contribute to its occurrence, like Hyperparathyroidism, Elevated calcium x phosphorus product, xerosis (dry skin caused by sweat gland atrophy), and Elevated serum magnesium and aluminum concentrations [5,9].

There have been theories put up that tie the immune and opioid systems into the process.

According to the immunological theory, systemic inflammation, not a localized skin condition, is what causes uremic pruritus [5]. The presence of T cells, pro-inflammatory cytokines like TNF, INF-Y, IL-2, and IL-6, as well as acute phase metabolites like C-reactive protein, in higher concentrations in hemodialysis patients with itching compared to those without it has been suggested to play a direct role in the development of pruritus [5].

According to the immune system theory, a rise in the ratio of Th1 and Th2 cells results in pruritus. According to theory, Th1 cells activate cytokines and inflammatory cells to generate pruritus, while Th2 cells secrete anti-inflammatory cytokines [6].

The opioid system hypothesis suggests that uremic pruritus results from over-expression of opioid receptors in skin cells and lymphocytes [10].

Numerous elements are believed to be involved in its development, even if the etiology is not fully known. Increased blood urea nitrogen (BUN), calcium, and phosphorus are some of these risk variables that predispose. Along with excessive vitamin A levels and related pathologies such as ascites, neurological disorders, and heart failure, it also contributes to the pathogenesis of the serum levels of magnesium, aluminum, B2 microglobulin, and histamine. Pruritus may also be caused by abnormal innervation, nerve injury, and central sensitization [13,14]. Pruritus is also influenced by genetic predisposition, particularly HLA-B35 [13,14].

The development of uremic pruritus is assumed to be influenced by dry skin despite several attempts to identify its risk factors. In 33–40% of patients, some investigations found an association between pruritus and xerosis and premature skin aging [15,16,17]. Some patients claim that their itching condition worsens during their dialysis treatments, whereas in other circumstances, the itching seems to get better.

Severe itching has been identified as a separate risk factor for higher morbidity and a bad prognosis [30]. Pruritus often causes worry, sadness, and sleep disruption. Heat, dehydration, and perspiration should all be avoided. Numerous studies have shown that itching goes away and kidney function is restored following kidney transplantation [11,12,13]. Antihistamines that are sedating offer a brief benefit; however, non-sedating antihistamines and topical steroids frequently fail to work [9, 14].

It has also been noted that improving the quality of blood transfusion, increasing its effectiveness, using a low-calcium and magnesium dialysate fluid, reducing the level of phosphorus calcium, and using more biocompatible membranes such as polymethylmethacrylate reduces the severity of itching or leads to its disappearance [31].

Emollients are used as the initial form of therapy, particularly those that contain linoleic acid, glycolic acid, and paraffin [18]. Capsaicin is helpful, according to studies, because it depletes substance P from C fibers, which prevents the transmission of pain and itching sensations. Topical cream containing 0.025% is used four times per day [19]. The anti-opioid medication nalfurafine is also beneficial in treating pain, according to studies [20]. It has been shown that narrowband UVB phototherapy can lower skin phosphorus levels and decrease lymphocyte production of cytokines [21].

Most studies investigating the prevalence of UP in HD patients were conducted in the Western world, and less data were available in the Middle East despite the high prevalence of ESRD in our community. Therefore, this study's main goal is to look into how common pruritus is among ESRD patients receiving hemodialysis at Tishreen University Hospital in Lattakia, Syria, between 2022 and 2023.

The secondary goal is to investigate the association of itching with the following laboratory indicators: phosphorus, calcium, and CaXP, as well as the association of itching with the duration of hemodialysis, the type of anticoagulant used during the hemodialysis session, and the Kt/V value.

2. Methods

2.1. Patients and Study Design

This observational descriptive cross-sectional study took place at a Lattakia, Syria, dialysis department at Tishreen University Hospital between January 2022 and May 2023. Hemodialysis patients who underwent treatment for at least 12 months were required to receive it four hours per day, two days per week. Patients' ages ranged from 18 to 74 years, with a mean of 46.77±14.9 years. There are no communication problems. Acute Kidney Injury patients receiving hemodialysis treatment and peritoneal dialysis patients were excluded due to additional diseases that cause pruritus, such as skin conditions, cancers, psychological disorders, and liver diseases, as well as an active infection.

HD was the method used for dialysis. (BRAUN and Fresenius) There were two different types of dialysis equipment. 200 patients in total agreed to participate and developed the inclusion criteria. After receiving ethical approval from the hospital's ethics committee, the dialysis center approved their participation.

The patients were informed of the study's goal. Then, the participants gave us their written approvals.

2.2. Data Collection and Procedure

During the HD sessions, the data collection forms were gathered personally. Patients' consent was obtained prior to data collection after we gave them a thorough explanation of the study. The patients were questioned regarding their socio-demographic information, clinical traits, and medical background. The intensity of itching was measured using a Visual Analog Scale (VAS). From hospital records, biochemical indications were gathered.

2.3. Identification of Uremic Pruritus

UP was identified as pruritus lasting more than three months with a VAS score of 4 or more, where 0 means no pruritus and 10 severe discomforting pruritus.

2.4. Patient Characteristics Form

The form for patient characteristics was created and reproduced after a review of the relevant literature. The socio-demographic and clinical characteristics of the patients are covered in this data. Age and gender were among the socio-demographic variables. The medical information included Kt/V, medication intake, CKD reasons, the length of hemodialysis per year, and various anticoagulants used.

2.5. Data Collection Form for Pruritus Status

The pruritus status data collecting form specified the following factors: the primarily afflicted area (facial, neck, back, abdomen, arm, leg, or full body); timing of itching, such as whether it occurs before or after hemodialysis; the severity of pruritus using VAS; and drugs used to relax pruritus.

2.6. Visual Analog Scale

In this study, the VAS is the primary rating method utilized to determine the severity of UP. VAS is used to convert non-numerically calculable values into numerical ones. The numerical values are spaced at intervals of one centimeter.

The VAS is a 10-point scale, with 0 denoting no pruritus and 10 denoting extremely severe itch.

The degree of pruritus was categorized as follows: 4 points were considered mild, 4 points but 7 points were moderate, 7 points but 9 points were severe, and 9 points were very severe.

2.7. Data Collection form for Biochemical Characteristics

Kt/V values, blood urea (BUN), calcium, phosphorus, and CaxP were the biochemical indicators that we recorded. Every month, the dialysis facility routinely completes these demanding measurements. Measurements were made of recent biochemical indicators. Using the Daugirdas formula, the Kt/V value was calculated. Kt/V and URR have 1.4 and 70% goals the Hemodialysis Adequacy 2006 Work Group authorized. According to the Kt/V levels of 1, 1.2, and 1.4, the patients in this study were split into 3 groups.

2.8. Statistical Analysis

Applying the rules of descriptive statistics to the variables under investigation. Quantitative variables with both central tendency and dispersion metrics. Variables of a qualitative nature with frequencies and percentages. The association between qualitative factors was investigated using the Chi-Square test.

The One-way ANOVA test examined the variations in means between various independent groups. With a 0.05 p-value, the results were deemed statistically significant. Use IBM SPSS Statistics Version 20 to compute statistical coefficients and evaluate the outcomes.

3. Results

3.1. Patient Characteristics

This study found that 72.5% of patients had pruritus (Table 1). The mean±SD age of the patients with pruritus was 46.77±14.9 years (Table 2). 58% of the study samples were males (Table 3). 83% of the studied research samples were within the age group of more than 30 years (Table 3). The mean±SD HD treatment duration was 3.66±2.7 years in patients with severe pruritus (Table 4).

Table 1. The prevalence of pruritus

Characteristic Pruritus present	Result
No Pruritus	55 (27.5%)
Mild	48 (24%)
Moderate	83 (41.5%)
Severe	10 (5%)
Very severe	4 (2%)

Table 2. The average age of the study sample

Age	MILD	MODERATE	SEVERE	VERY SEVERE	P-value
Mean ± SD	44.23±11.4	48.61±13.4	50.60±16.3	62.12±9.8	0.02
Min – Max	27-61	25-74	35-72	18-73	

Table 3. The demographic characteristics of the study sample

Variable	Result
Gender	
Male	(58%)
Female	84 (42%)
age groups	
<30	34 (17%)
>30	166 (83%)

Table 3.1. The demographic characteristics of the study sample

GENDER	MILD	MODERATE	SEVERE	VERY SEVERE	*P-value
Male	30(62.5%)	43(51.8%)	6(60%)	2(50%)	0.06
Female	18(37.5%)	40(48.2%)	4(40%)	2(50%)	

**p-value is significant at < 0.05 level. There were no statistically significant differences between the severity of itching and gender, p>0.05.*

Table 4. The HD duration treatment

DURATION OF DIALYSIS	MILD	MODERATE	SEVERE	VERY SEVERE	P-value
Mean ± SD	4.02±1.2	3.92±1.5	3.66±2.7	2.45±1.9	0.03
Min – Max	1-10	1-9	1-12	1-7	

**p-value is significant at < 0.05 level*

3.2. Prevalence and Characteristics of Uremic Pruritus

The descriptive characteristics of patients with pruritus are shown in the Tables below (Table5,6,7). The pruritus affected the entire body (Generalized) in 95 patients, with most preset mild pruritus at 91.7%. There were no differences in the severity of itching before and after hemodialysis. 41.5% of patients showed moderate pruritus, and 2% had severe pruritus. 100% of patients with mild and moderate pruritus used calcium and VD. In addition, 100% of patients who had very severe pruritus used Analgesics for their pruritus.

3.3. Characteristics Related to the Dialysis Device

Patients who used the Braun device had a milder severity of itching. In addition, the longer the dialysis period, the less severe the itching (Table 9).

The Kt/V was 1.4 in 80 patients, 96.4%, who experienced moderate pruritus (Table 10). We discovered that using low molecular weight heparin during the hemolysis session reduced itching severity (Table 11).

Table 5. The body area affected by pruritus

Itchy place	MILD	MODERATE	SEVERE	VERY SEVERE	P-value
Limbs	0(0%)	13(15.7%)	2(20%)	1(25%)	0.09
Chest	0(0%)	3(3.6%)	0(0%)	0(0%)	
Generalized	44(91.7%)	47(56.6%)	3(30%)	1(25%)	
Back	0(0%)	7(8.4%)	1(10%)	0(0%)	
Face	0(0%)	7(8.4%)	0(0%)	0(0%)	
Hands	4(8.3%)	3(3.6%)	0(0%)	1(25%)	
Palms and soles	0(0%)	3(3.6%)	2(20%)	0(0%)	
Feet	0(0%)	0(0%)	2(20%)	1(25%)	

Table 6. Timing of pruritus

Pruritus timing	MILD	MODERATE	SEVERE	VERY SEVERE	P-value
Before dialysis	40(83.3%)	31(37.3%)	7(70%)	0(0%)	0.06
After dialysis	8(16.7%)	52(62.7%)	3(30%)	4(100%)	

Table 7. Medications intake of pruritus

medications intake	MILD	MODERATE	SEVERE	VERY SEVERE	P-value
CALCIUM	48(100%)	83(100%)	6(60%)	2(50%)	0.002
Vitamin D	48(100%)	83(100%)	7(70%)	1(25%)	0.0001
Urate lowering therapy	8(16.7%)	21(25.3%)	3(30%)	0(0%)	0.4
Phosphorus chelator	0(0%)	0(0%)	3(30%)	1(25%)	0.2
Antihistamine	44(91.7%)	78(94%)	6(60%)	4(100%)	0.09
Analgesic	0(0%)	0(0%)	7(70%)	4(100%)	0.001

None of the Causes of chronic kidney disease had a statistically significant effect on pruritus development (Table 8).

Table 8. The most common causes of CKD in the study sample

Diseases causing chronic kidney disease	Number of patients	Percentage	MILD	MODERATE	SEVERE	VERY SEVERE	P-value
High blood pressure	75	37.5%	40(83.3%)	33(39.8%)	2(20%)	0(0%)	0.06
Stones	33	16.5%	0(0%)	10(12%)	3(30%)	0(0%)	
Hereditary	17	8.5%	4(8.3%)	11(13.3%)	0(0%)	0(0%)	
unknown reasons	16	8%	0(0%)	7(8.4%)	0(0%)	3(75%)	
Diabetes	15	7.5%	0(0%)	7(8.4%)	3(30%)	1(25%)	
Glomerulonephritis	13	6.5%	0(0%)	9(10.8%)	2(20%)	0(0%)	
Medications	11	5.5%	4(8.3%)	3(3.6%)	0(0%)	0(0%)	
Preeclampsia	10	5%	0(0%)	3(3.6%)	0(0%)	0(0%)	

Table 9. Type of the hemodialysis machine

TYPE OF DIALYSIS DEVICE	MILD	MODERATE	SEVERE	VERY SEVERE	P-value
Fresenius	48(100%)	75(90.4%)	5(50%)	3(75%)	0.0001
BRAUN	0(0%)	8(9.6%)	5(50%)	1(25%)	

3.4. Properties Related to Laboratory Indicators

Increased blood urea, calcium, and phosphorus were associated with increased itching severity. In addition, an increase in CaXP was associated with an increase in itching severity.

Table 10. Kt/V values

Kt/V	MILD	MODERATE	SEVERE	VERY SEVERE	P-value
1	0(0%)	3(3.6%)	0(0%)	1(25%)	0.0001
1.2	0(0%)	0(0%)	7(70%)	3(75%)	
1.4	48(100%)	80(96.4%)	3(30%)	0(0%)	

Table 11. Anticoagulant type that is used during dialysis sessions

Type of Anticoagulant	MILD	MODERATE	SEVERE	VERY SEVERE	P-value
HEPARIN	44(91.7%)	80(96.4%)	8(80%)	3(75%)	0.0001
***LMWH**	4(8.3%)	3(3.6%)	2(20%)	1(25%)	

**low molecular weight heparin*

Table 12. Laboratory indicators

LABORATORY INDICATORS	MILD	MODERATE	SEVERE	VERY SEVERE	P-value
blood urea	111.62±25.7	120.84±42.7	137.1±19.5	139.3±24.4	0.01
Calcium	6.96±0.8	8.24±0.9	8.52±3.8	8.87±0.4	0.0001
Phosphorus	6.42±1.6	7.08±1.7	8.30±0.6	9.22±0.3	0.0001
CaXP	46.49±21.2	58.81±18.9	67.32±23.4	78.18±11.8	0.0001

**CaXP: calcium Phosphorus product*

4. Discussion

This study aimed to determine how frequently hemodialysis (HD) patients experienced uremic pruritus. Although UP is a typical and frequently serious sign of HD, its underlying pathophysiological process is not entirely understood. In medical literature, UP can be found anywhere between 50% and 90% of the time [5]. Some studies in the medical literature suggest that the prevalence of pruritus in HD patients may decrease with more effective dialysis [5].

This study showed that 72.5% of HD patients had UP. Differences in the prevalence were observed among countries. The differences in the prevalence data may be due to the different study designs, selection of participants (e.g., study populations, races, and sample sizes), and the definition of pruritus in the included studies. For example, in the United States, Duque et al. conducted a cross-sectional study including 105 HD participants and discovered that the prevalence of pruritus was 57.1% [22]. Meanwhile, Gatmiri et al. studied 99 HD patients in Iran and found that the prevalence was 58.6% [23]. Participants' ages ranged from 18 to 74 years old, with a 46.77±14.9 average age. There was no statistically significant correlation between gender and pruritus severity in our investigation, although, in other studies, the severity of pruritus was slightly higher in males than in females.

Regarding the intensity of the itching, we found that 24% of our patients had mild itching, 41.5 % had moderate itching, 5% had severe itching, and 2% had really severe itching. The study discovered a strong correlation between blood urea nitrogen (BUN), serum calcium, and phosphorus levels and the severity of UP. Patients with moderate pruritus had higher levels of BUN (120.84±42.7 mg/dL), patients with severe pruritus had higher levels of serum calcium (8.52±3.8 mg/dL), and patients with very severe pruritus had higher levels of serum phosphorus (9.22±0.3 mg/dL) and calcium-phosphate product (CaXP) (78.18±11.8 mg/dL2).

Due to inadequate analysis, the study did not investigate the association between the severity of UP and serum parathyroid hormone (PTH) levels; nevertheless, this relationship has been studied in previous studies. The results of this research showed that taking calcium and vitamin D supplements worsened pruritus because too much calcium can cause calcium phosphate crystals to accumulate more quickly [5]. While other studies have found a substantial correlation between UP severity and diabetes, hypertension, hyperphosphatemia, and the causes of chronic kidney disease (CKD), we could not detect any links between UP severity and any of these conditions.

There was no correlation between UP severity and age in our investigation, in contrast to results from other studies that have demonstrated a substantial relationship between UP severity and advancing age. However, elderly patients with very acute pruritus may have more advanced skin conditions, including dry skin brought on by sweat gland atrophy, decreased skin elasticity, and a reduced need for emollients [5, 6].

In the UK, 54% of CKD-associated pruritus patients felt that their quality of life was significantly impacted [24], according to Kosmadakis et al. In this study, the Braun device performed less well than other dialysis systems at reducing pruritus. This could result from the different types

of dialysis tubes being utilized and a psychological component in the patient.

This study found that in HD patients, the clearance of small and middle-sized molecules was inversely correlated with the severity of UP. This aligns with earlier research [25, 26] that revealed a range of uremic toxins might act as pruritogenic agents. Longer dialysis sessions enhance patients' quality of life and lessen pruritus intensity. This may be explained by individuals with longer dialysis histories having higher Kt/V values, indicators of the procedure dose. In addition, lengthier dialysis sessions mean more time spent in contact with silicone tubing and dialysis membranes, which assist in lowering lower blood levels of uremic toxins [5].

In addition, this research discovered that using low-molecular-weight heparin (LMWH) reduced pruritus. This may be because LMWH inhibits T lymphocytes' ability to produce heparanase, which is crucial for T cells to migrate to their target organs. A low dose of LMWH, such as enoxaparin, efficiently alleviates pruritus. Because enoxaparin has a higher bioavailability, it may be more effective in treating lichen planus, according to certain research [5].

The advantage of this study is that it is the first one to indicate the prevalence of pruritus in hemodialysis patients and its correlation with laboratory outcomes and dialysis features in Lattakia, Syria. Some restrictions apply to the study. The sample size, for instance, is modest. The findings cannot be applied to the entire population of Syria because data were only gathered from one center. According to the use of only one type of membrane, polyethersulfone, we were unable to analyze the correlation between itching and the dialysis membrane used.

Due to employing the same sterilization method—thermal-chemical sterilization—on all devices, the study was unable to analyze the correlation between itching and the kind of device sterilization. Because of using a single type of dialysis fluid, we were unable to analyze the correlation between pruritus and dialysis fluid. Due to the complexity of the analysis, no studies have been done on the association between itching and parathyroid hormone. We only looked at pruritus in HD patients because our clinic did not employ PD treatment. Other research evaluated the uremic pruritus characteristics between PD and HD patients. According to a study on Taiwanese peritoneal dialysis patients, less inflammation is induced, as seen by the decreased production of IL-6 and CRP, compared to patients receiving HD [27, 28].

Compared to PD patients, HD patients exhibited much more severe CKD-associated pruritus, according to Wu et al. [29], although Mistik et al. [30] reported the opposite. While we did not include skin conditions in our analysis, an Indian investigation of mucocutaneous symptoms in people with chronic renal illness discovered a correlation between xerosis severity and itching severity [31]. The main factors contributing to the severity of xerosis are skin dehydration, diuretics, hypervitaminosis A, decreased sweat/sebum excretion, altered skin barrier, and lack of emollient use. Pharmaceutical or non-pharmacological strategies to enhance the management of pruritus can be the subject of future research. HD patients' immune systems' five components continue to be a fascinating subject that merits more research.
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5. Conclusion

In HD patients, pruritus is common, according to our study. The most significant risk factor for the emergence of itching, according to our research, is greater phosphorus levels. Consequently, we advise giving measured dosages of calcium and vitamin D. getting Kt/V to the highest possible value. Blood urea, calcium, phosphorus, magnesium, and parathyroid hormone should all be monitored on a regular basis. Educate the patient on the need to preserve elastic skin to avoid exposure to high heat and dryness, and do not ignore any skin issues.

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References

[1] Theodor W. Post, and Burton D. Rose, "Overview of the Management of Chronic Kidney Disease in Adults," *Up to Date*, 2007. [Google Scholar]

[2] Mario Bonomini et al., "New Treatment Approaches for the Anemia of CKD," *American Journal of Kidney Diseases*, vol. 67, no. 1, pp. 133-142, 2016. [CrossRef] [Google Scholar] [Publisher Link]

[3] Lesley A. Stevens et al., "Assessing Kidney Function-Measured and Estimated Glomerular Filtration Rate," *New England Journal of Medicine*, vol. 354, pp. 2473-2483, 2006. [CrossRef] [Google Scholar] [Publisher Link]

[4] Jonathan Himmelfarb, and T. Alp Ikizler, "Hemodialysis," *New England Journal of Medicine*, vol. 363, pp. 1833-1845, 2010. [CrossRef] [Google Scholar] [Publisher Link]

[5] Sidney M. Kobrin, "Uremic Pruritus," *Up to Date*, 2017. [Google Scholar] [Publisher Link]

[6] Nurten Ozen et al., "Uremic Pruritus and Associated Factors in Hemodialysis Patients: A Multi-Center Study," *Kidney Research and Clinical Practice*, vol. 37, no. 2, pp. 138-147, 2018. [CrossRef] [Google Scholar] [Publisher Link]

[7] Tejesh S. Patel, Barry I. Freedman, and Gil Yosipovitch, "An Update on Pruritus Associated with CKD," *American Journal of Kidney Diseases*, vol. 50, no. 1, pp. 11-20, 2007. [CrossRef] [Google Scholar] [Publisher Link]

[8] Murphy, and Carmichael, "Renal Itch," *Clinical and Experimental Dermatology*, vol. 25, no. 2, 103-106, 2000. [CrossRef] [Google Scholar] [Publisher Link]
[9] Jacek C. Szepietowski et al., "Uremic Pruritus: A Clinical Study of Maintenance Hemodialysis Patients," *The Journal of Dermatology*, vol. 29, no. 10, pp. 621-627, 2002. [CrossRef] [Google Scholar] [Publisher Link]
[10] Richard J. Johnson et al., *Comprehensive Clinical Nephrology*, 9th ed., Elsevier Health Sciences, pp. 1-1312, 2018. [Google Scholar] [Publisher Link]
[11] Julia R. Nunley et al., "Dermatologic Manifestations of Renal Disease," *Dermatology*, 2020. [Google Scholar] [Publisher Link]
[12] P. Udayakumar et al., "Cutaneous Manifestations in Patients with Chronic Renal Failure on Hemodialysis," *Indian Journal of Dermatology, Venereology and Leprology*, vol. 72, no. 2, pp. 119-125, 2006. [CrossRef] [Google Scholar] [Publisher Link]
[13] Arshad Jamal, and P.T.Subramanian, "Pruritus among End-Stage Renal Failure Patients on Hemodialysis," *Saudi Journal of Kidney Diseases and Transplantation*, vol. 11, no. 2, pp. 181-185, 2000. [Google Scholar] [Publisher Link]
[14] Sanzida S. Swarna et al., "Pruritus Associated with Chronic Kidney Disease: A Comprehensive Literature Review," *Cureus*, vol. 11, no. 7, pp. 1-6, 2019. [CrossRef] [Google Scholar] [Publisher Link]
[15] Eman Sanad et al., "Prevalence of Cutaneous Manifestations in Chronic Renal Failure Patients on Regular Hemodialysis: A Hospital-Based Study," *Egyptian Journal of Dermatology and Venerology*, vol. 34, no. 1, pp. 27-35, 2014. [CrossRef] [Google Scholar] [Publisher Link]
[16] Maha M. Sultan et al., "Cutaneous Manifestations in Egyptian Patients with Chronic Renal Failure on Regular Hemodialysis," *Egyptian Women Dermatologic Society*, vol. 27, no. 1, pp. 49-55, 2010. [Google Scholar] [Publisher Link]
[17] Jacek C. Szepietowski, Adam Reich, and Robert A. Schwartz, "Uremic Xerosis," *Nephrol Dial Transplant*, vol. 19, no. 11, 2709-2712, 2004. [CrossRef] [Google Scholar] [Publisher Link]
[18] Yung-Chih Chen, Wan-Ting Chiu, and Mai-Szu Wu, "Therapeutic Effect of Topical Gamma-Linolenic Acid on Refractory Uremic Pruritus," *American Journal of Kidney Diseases*, vol. 48 no. 1, pp. 69-76, 2006 .[CrossRef] [Google Scholar] [Publisher Link]
[19] Atieh Makhlough et al., "Topical Capsaicin Therapy for Uremic Pruritus in Patients on Hemodialysis," *Iranian Journal of Kidney Diseases*, vol. 4, no. 3, pp. 173-140, 2010. [Google Scholar] [Publisher Link]
[20] Shigeki Inui, "Nalfurafine Hydrochloride to Treat Pruritus: A Review," *Clinical, Cosmetic and Investigational Dermatology*, vol. 8, no. 5, pp. 249-255, 2015. [CrossRef] [Google Scholar] [Publisher Link]
[21] Pentamveli Beegum Sherjeena et al., "A Controlled Trial of Narrowband Ultraviolet B Phototherapy for the Treatment of Uremic Pruritus," *Indian Journal of Dermatology, Venereology, and Leprology*, vol. 83, no.2, pp. 247-249, 2017. [CrossRef] [Google Scholar] [Publisher Link]
[22] M.I. Duque et al., "Uremic Pruritus is Associated with Higher kt/V and Serum Calcium Concentration," *Clinical Nephrology*, vol. 66, no. 3, pp. 184-191, 2006. [CrossRef] [Google Scholar] [Publisher Link]
[23] Seyed Mansour Gatmiri et al., "Uremic Pruritus and Serum Phosphorus Level," *Acta Medica Iranica*, vol. 51, no. 7, pp. 477-481, 2013. [Google Scholar] [Publisher Link]
[24] George Ch. Kosmadakis et al., "Characteristics of Uremic Pruritus in Hemodialysis Patients: Data from a Single Center," *Kidney International*, vol. 74, no. 7, pp. 962-973, 2008. [CrossRef] [Google Scholar] [Publisher Link]
[25] I. Narita et al., "Etiology and Prognostic Significance of Severe Uremic Pruritus in Chronic Hemodialysis Patients," *Kidney International*, vol. 69, no. 9, pp. 1626-1632, 2006. [CrossRef] [Google Scholar] [Publisher Link]
[26] Mei-Ju Ko et al., "Uremic Pruritus, Dialysis Adequacy, and Metabolic Profiles in Hemodialysis Patients: A Prospective 5-Year Cohort Study," *PLOS ONE*, vol. 8, no. 8, pp. 1-8, 2013. [CrossRef] [Google Scholar] [Publisher Link]
[27] Marion Haubitz et al., "Chronic Induction of C-Reactive Protein by Hemodialysis, But Not By Peritoneal Dialysis Therapy," *Peritoneal Dialysis International*, vol. 16, no. 2, pp. 158-162, 1996. [CrossRef] [Google Scholar] [Publisher Link]
[28] Toshimasa Takahashi et al., "Interleukin-6 Gene Expression in Peripheral Blood Mononuclear Cells from Patients Undergoing Hemodialysis or Continuous Ambulatory Peritoneal Dialysis," *Renal Failure*, vol. 22, no. 3, pp. 345-354, 2000. [CrossRef] [Google Scholar] [Publisher Link]
[29] Hon-Yen Wu et al., "A Comparison of Uremic Pruritus in Patients Receiving Peritoneal Dialysis and Hemodialysis," *Medicine*, vol. 95, no. 9, pp. 1-6, 2016. [CrossRef] [Google Scholar] [Publisher Link]
[30] S. Mistik et al., "An Epidemiology Study of Patients with Uremic Pruritus," *Journal of the European Academy of Dermatology and Venereology*, vol. 20, no. 6, pp. 672-678, 2006. [CrossRef] [Google Scholar] [Publisher Link]
[31] Omar Lupi et al., "Cutaneous Manifestations in End Stage Renal Disease," *Anais Brasileiros De Dermatologia*, vol. 86, no. 2, pp. 319-326, 2011. [CrossRef] [Google Scholar] [Publisher Link]