Frequency and possible pathogenesis of chronic renal failure-associated pruritus in dialyzed patients

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Background
Uremic pruritus is a common dermatological problem in patients on hemodialysis. The pathogenesis is not fully understood; it is a multifactorial infection. The aim of this study was to identify the frequency of pruritus in patients with chronic renal failure on hemodialysis and its association with serum electrolytes (Ca and P), level of parathyroid hormones (PTH), and dialysis adequacy.

Patients and methods
A total of 60 patients with chronic renal failure on hemodialysis were included in the present study from dialysis unit in the Faculty of Medicine, Assuit University Hospital. Data were collected according to a structural questionnaire, including age, sex, and duration of dialysis. The authors investigated sociodemographic data, and several biochemical tests, such as calcium, phosphorus, kidney functions, and PTH, were performed to know their association with uremic pruritus. All patients,from them is corrected and deleted it so the sentence become as follow: A detailed description of the study and written informed consent was obtained. The study was registered with IRB no.17101062.

Results
This study revealed that the prevalence of pruritus was higher in males than females, and also, there was no association with age. Of all biochemical tests, phosphorus, PTH, and duration of dialysis showed significant association with pruritus (P=0.043, 0.000, and 0.030, respectively). The association between PTH and the other study variables showed that significant association with calcium (P=0.012). The dialysis adequacy showed no significant association with other variables.

Conclusion
Uremic pruritus is a common problem, occurring in ~64.9% in patients with chronic kidney disease on hemodialysis. In this study, the authors found that increase in PTH level, increase in serum phosphorus, dialysis adequacy, and xerosis play a major role in pathogenesis of renal pruritus. The authors recommend from this study regular follow-up of patients treated for more than 6 months with hemodialysis, with regular measurement of PTH level and serum phosphorus and their proper management to prevent appearance of renal pruritus and use of novel approaches such as tacrolimus ointment, oral activated charcoal, phototherapy, acupuncture, and kidney transplantation.

Keywords:
parathyroid hormones, pruritus, hemodialysis, uremic, electrolytes, urea reduction ratio

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Introduction

Globally, kidney disease affects more than 750 million persons. It is a known public health problem [1]. Chronic renal failure (CRF) is defined according to the degree of kidney damage and loss of function over a period of months or years. All individuals with glomerular filtration rate less than 60 ml/min/1.73 m^2 for 3 months or more are categorized as having chronic kidney disease[2] Kidney failure is also called end-stage renal disease. Patients on hemodialysis, have moderate to severe pruritus, often feel depressed and drained, have a 17% higher mortality rate, and have a poor quality of sleep [3]. There are several causes of CRF such as diabetic nephropathy, hypertension, glomerulonephritis, interstitial nephritis, pyelonephritis, polycystic kidney disease, and obstructive nephropathy [4]. CFR is linked to several complications, including electrolyte disturbances (hyperphosphatemia and hypocalcemia), hyperparathyroidism, anemia, and cutaneous complications (uremic pruritus) [5].

Uremic pruritus is one of the most frequent and burdensome symptoms in patients with kidney failure, affecting up to 46% of hemodialysis patients [6]. Uremic pruritus can be a generalized or localized itch affecting the back, face, and arms [7]. Uremic pruritus

has a multifactorial pathogenesis and is associated with physical disability, impaired quality of life, and mental limitations, such as anger, anxiety, and depression [8–10]. Uremic pruritus has been recognized as a fundamental research priority among the patients with kidney disease [11]. The actual mechanism of uremic pruritus and its association with CRF is poorly understood, but there are number of suspected causes that may play a role in the development of pruritus in patients with CRF such as hyperphosphatemia, hyperparathyroidism, immunohypothesis (interleukin-2 and interleukin-6), opioid hypothesis, histamine and serotonin receptors, inadequate removal of uremic toxins by dialysis, and neuropathic changes [12].

The main objective of the present study was to explore the frequency and possible relation between pruritus in patients with CRF on hemodialysis and different laboratory parameters such as serum electrolytes (Ca and P), level of parathyroid hormones (PTH), and dialysis adequacy that may help in understanding the pathogenesis of uremic pruritus.

Patients and methods

Study design and population

This cross-section study was conducted at the hemodialysis unit of the internal medicine department Assiut University. A total of 60 patients with CRF on hemodialysis for more than 6 months were included. Patients were divided into two group: group I included 30 patients with CRF with pruritus, and group II included 30 patients with CRF without pruritus. Inclusion criteria were patients with CRF and pruritus diagnosed by nephrologists. Exclusion criteria were patients with primary skin disease, cholestatic liver disease, acute hepatitis, parasitic infections, and malignancy. A detailed description of the study and written informed consent was registered with IRB No.17101062.

Data collection

The fundamental demographic and clinical data were collected by using a questionnaire containing several variables such as age, sex, duration of hemodialysis, assesses degree of skin affection as scratch marks, ulcers, and secondary infections to obtain information that would be of help to the study.

Biochemical testing

A number of biochemical tests for patients and controls were performed on the blood samples such as complete blood count, serum electrolytes (Ca^+ and P^+), PTH level, and dialysis adequacy using urea reduction ratio (URR), which were measured according to their respective kits' and manufacturers' instructions and their universal equations.

Statistical analysis

Statistical analysis was performed using statistical Package for the Social Sciences Version 16.0 for Window software (SPSS Inc. was a software house headquartered in Chicago and incorporated in Delaware). Mean and SD were used to express quantitative data. For continuous variable, testing between two groups was performed by the Mann–Whitney *U*-test. Categorical variables were compared by Pearson χ^2 test when very small proportions were analyzed. Correlations among continuous variables were calculated by the Spearman rank correlation coefficient (r_s). *P* values of less than 0.05 were considered statistically significant.

Results

Sociodemographic and clinical characteristics

Our study was conducted on the prevalence of chronic kidney disease-associated pruritus in the dialysis unit of internal medicine department of Assiut University Hospital and found the prevalence was 64.9% (Fig. 1). The mean ± standard deviation (SD) age was 44.30 ± 14.15 years for group I and 48.10 ± 17.65 years for group II. Males represented 17 (56.7%) and 13 were (43.3%) females in group I, and 18 (60%) were males and 12 (40%) were females in group II. A total of 20 (66.6%) patients in group I experienced xerosis or dry skin on clinical examination compared with 15 (50%) patients in group II. In group I, pruritus was severe generalized in five (16.6%), moderate in all extremities in 15 (50%), and mild limited to legs only in five (33.3%). The clinical diagnosis for any chronic diseases present was collected and is summarized in Table 1.

Duration of hemodialysis and biochemical parameters

Fig 1 shows the prevalence of chronic kidney disease-associated pruritus in the dialysis unit of internal medicine department of Assiut University Hospital.

Fig 2 shows the duration of hemodialysis for both groups. In group I, the mean duration was 5.88 ± 3.28, and it was 4.19 ± 2.61 in group II, with significant association (*P* = 0.030). In addition, measurements of electrolytes including calcium and phosphorus levels

Table 1 Sociodemographic data and clinical characteristics of patients with chronic renal failure on hemodialysis with and without pruritus

	Group I (*n*=30) [*n* (%)]	Group II (*n*=30) [*n* (%)]	*P*
Sex			
Male	17 (56.7)	18 (60.0)	0.793
Female	13 (43.3)	12 (40.0)	
Age (years)			
Mean±SD	44.30±14.15	48.10±17.65	0.554
Range	17.0-65.0	18.0-80.0	
Comorbidities			
HTN	23 (76.7)	15 (50.0)	0.032*
DM and HTN	4 (13.3)	2 (6.7)	0.667
PKD	0	5 (16.7)	0.062
Unknown	3 (10.0)	8 (26.7)	0.095

Data were presented as number and percentage, with *P<0.05 being significant. DM, diabetes mellitus; HTN, hypertension; PCKD, polycystic kidney disease.

Table 2 Serum electrolytes in patients with chronic renal failure on hemodialysis with and without pruritus

Electrolytes	Group I (*n*=30)	Group II (*n*=30)	*P*
Ca (mg/dl)			
Mean±SD	8.28±1.24	7.91±1.35	0.672
Range	6.0-11.6	4.5-10.6	
PO_4 (mg/dl)			
Mean±SD	5.91±2.14	4.92±1.60	0.043*
Range	1.2-11.6	1.2-7.8	

Data are presented as number and percentage, with *P<0.05 is significant. PO_4, phosphorus.

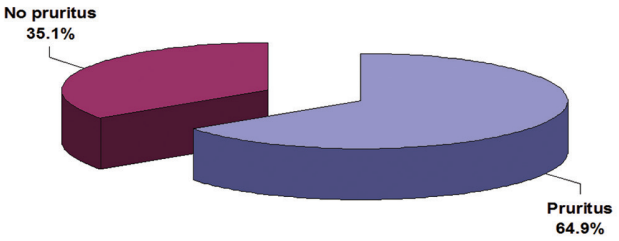
were performed and represented in Table 2. The mean hemoglobin level for both group I and group II was 9.87 ± 1.75 and 9.20 ± 1.38, respectively, without significant association with pruritus (P = 0.91). Assessments of PTH were performed and showed highly significant association with presence of pruritus (P = 0.000) (Fig. 3). The correlation between PTH in both groups and the other study variables was performed and showed varied positive and negative correlation. The correlation was not statistically significant, except for calcium, which showed a negative correlation with significant association (P = 0.012) in group I only. Data are summarized in Table 3.

Dialysis adequacy as determined by URR was performed and showed lower value in group I, with mean ± SD of 64.53 ± 4.57, than in group II, with positive correlation detected between dialysis adequacy by URR and pruritus (Figs. 3 and 4). Moreover, the correlation of dialysis adequacy and the other variables was performed and is summarized in Table 4.

Discussion

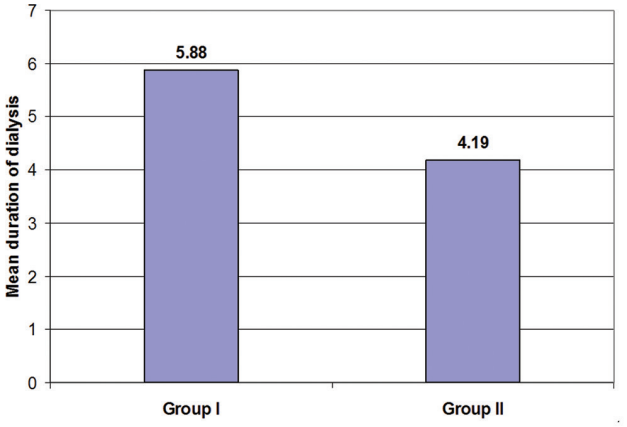
Dermal symptoms such as itching is associated with CRF, which cause changes in quality of life,

Figure 1



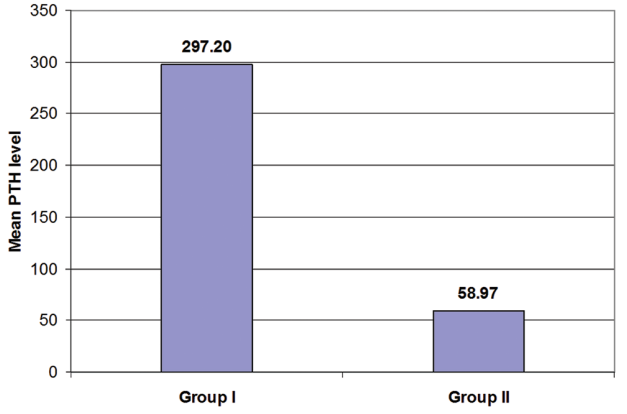
Prevalence of chronic kidney disease-associated pruritus in the Dialysis Unit of Internal Medicine Department of Assiut of University Hospital.

Figure 2



Mean duration of dialysis for patients with and without pruritus.

Figure 3



Parathyroid hormones level in patients with chronic renal failure on hemodialysis with and without pruritus.

anxiety and depression symptoms, which increase the morbidity risk [13]. The association between the dermal symptoms and morbidity rate in renal patients showed that patients with pruritus have a high morbidity rate of 23% more than the patient without itching [13]. Our study aimed to identify the prevalence and association between pruritus in patients with CRF on hemodialysis and several laboratory tests, such as serum electrolytes (Ca and P), level of PTH,

Table 3 Correlations of parathyroid hormones level with other variables in patients with chronic renal failure on hemodialysis with and without pruritus

Variables	PTH			
	Group I		Group II	
	r	*P*	*r*	*P*
Age (years)	−0.309	0.096	0.015	0.937
Duration of dialysis (years)	0.161	0.394	−0.040	0.832
Hb (g/dl)	0.039	0.839	0.135	0.477
Serum urea (mmol/l)	0.175	0.355	−0.056	0.769
Serum creatinine (μmol/l)	0.071	0.711	−0.005	0.977
Ca (mg/dl)	−0.453	0.012*	0.086	0.652
PO_4 (mg/dl)	0.110	0.561	0.074	0.698
eGFR (ml/min1.73 m^2)	−0.064	0.738	−0.059	0.755

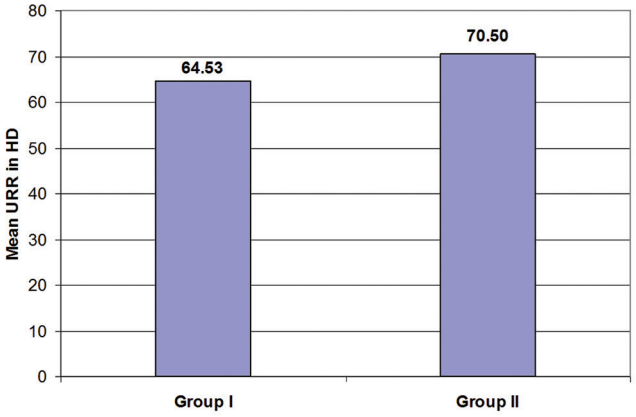
*P<0.05, significant. eGFR, estimated glomerular filtration rate; Hb, hemoglobin; PTH, parathyroid hormones; *R* value: regression value.

Table 4 Correlations of dialysis adequacy with other variables in group II (patients with chronic renal failure without pruritus)

Variables	URR%	
	r	*P*
Age (years)	−0.141	0.457
Duration of dialysis (years)	−0.005	0.978
Hb (g/dl)	0.181	0.339
Serum urea (mmol/l)	0.094	0.622
Serum creatinine (μmol/l)	0.143	0.451
Ca (mg/dl)	0.081	0.669
PO_4 (mg/dl)	0.021	0.911
eGFR (ml/min/1.73 m^2)	−0.077	0.686

eGFR, estimated glomerular filtration rate; Hb, hemoglobin; URR, urea reduction ratio.

Figure 4



Mean dialysis adequacy in patients with chronic renal failure with and without pruritus.

and dialysis adequacy to help in understanding the pathogenesis of uremic pruritus.

In the present study, the prevalence of pruritus was slightly higher in males than females. The difference in pruritus prevalence according to sex was not statically significant (P = 0.793). Our study findings were in the line with Mistik *et al.*[14] and Pisoni *et al.* [15], who reported that males had a greater susceptibility of having pruritus from moderate to severe. This was in contrast with Szepietowski *et al.*[16] and Dar *et al.* [17], who reported a higher prevalence in females than males. In the present study, there was no significant association with age (P = 0.554). This result is in agreement with Suzuki *et al.* [5]. On the contrary, Weiss *et al.*[18] reported that the prevalence of pruritus has a higher prevalence in patients aged greater than 70 years. The difference may owing to our study population with pruritus having an age range from 17.0 to 65.0 years. In the present study, there were several comorbidities in association with pruritus including hypertension, diabetes mellitus, and polycystic kidney disease, and significant association was showed in case of hypertension. Our study reported that there was a significant association between pruritus and dialysis duration, which agrees with previous studies [19,20]. Our study findings showed that there were no significant associations between pruritus and kidney function parameters, including urea, creatinine, and estimated glomerular filtration rate as well as hemoglobin level. Moreover, the levels of calcium and phosphorus showed variation in patients with CRF with and without pruritus. The difference was significant between pruritus and phosphorus (P = 0.043), which agrees with Gatmiri *et al.* [21]. In the present study, PTH showed highly significant association with pruritus (P = 0.000). Our study findings are in agreement with Narita *et al.* [22], who reported a significant association between PTH levels and pruritus. The association between PTH and other study variables showed that only calcium has a significant association and negative correlation in patients with pruritus (P = 0.012). In our study, there was no significant association between hemoglobin level and pruritus. The dialysis adequacy in the present study showed no significant association with the other study variables.

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Conflicts of interest
There are no conflicts of interest.

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