

# Pruritus in hemodialysis patients: Results from Fresenius dialysis center, Banja Luka, Bosnia and Herzegovina

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## ABSTRACT

**Introduction:** Uremic pruritus (UP) is a common and distressing complication of end-stage renal disease (ESRD). A global cross-sectional study of 18,000 hemodialysis patients reported a 42% prevalence of moderate or extreme UP, which was strongly associated with sleep disturbance, depression, impaired quality of life, and mortality. Pruritus is commonly encountered in individuals with end-stage renal disease (ESRD) on hemodialysis (HD). **Materials and Methods:** This cross-sectional study was performed in order to find out the prevalence of pruritus in patients on regular maintenance hemodialysis (HD) as well as to analyze its relationship to age, sex of the patient, duration of hemodialysis in months per patient, serum levels of phosphate, PTH, KT/V (index of dialysis dose), parameters in the beginning of the study and six months after. The data were analyzed by descriptive statistics-Wilcoxon Signed Rank Test and Chi-square test with Yates correction factor. **Results:** Sixty and two patients with ESRD (age ranging from 31 to 87 years) free from systemic, skin or psychiatric disorders and other secondary causes attributable to pruritus, undergoing maintenance HD (duration on HD 4-348 months; mean 86.97 and median 79,5 months) at Fresenius dialysis center, Banja Luka, Bosnia and Herzegovina were evaluated for pruritus. Pruritus has been discovered in 21 out of 34 males (54,8%) and 6 out of 28 females (22,2%). Our study as many others showed that pruritus is very common (45.2%) in HD patients. Applying  $\chi^2$  test with Yates correction factor is highly statistically significant ( $\chi^2 = 8.003$ ,  $p = 0.005$ ) by gender. Research of the gender revealed that pruritus appeared more in men analysis. There were no significant differences between other measured markers: to age, duration of hemodialysis in months per patient, serum levels of phosphate, PTH, KT/V (index of dialysis dose) in patients with pruritus and in patients without pruritus. **Conclusions:** This first cross-sectional study describes key features UP in Republic of Srpska (Bosnia and Herzegovina) and results that the UP is significantly more common in men. This study demonstrates that the serum level of PTH and phosphate isn't associated with the incidence of pruritus in HD patients.

**Key words:** Uremic pruritus; End-stage renal disease; Hemodialysis

## INTRODUCTION

Pruritus, defined as an unrestricted and uncomfortable sensation that elicits the desire to scratch, has been well recognized as a common complication in patients with chronic Renal failure [2-6]. It has been found that 15%-49% of patients with predialysis chronic renal failure

and 50%-90% of those on hemodialysis or CAPD have pruritus [7].

In 2012, over 2500 patients received hemodialysis (HD) in the Bosnia and Herzegovina [17], in USA about 384,000 [7], and in Germany about 63,300 patients per year depend on HD [8]. It is estimated that worldwide

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more than 2 million people suffer from end-stage renal disease (ESRD) that requires HD.

Pruritus may be localized or disseminated and is the most common symptom of ESRD. It occurs in about 53% of these patients, causing great harm to their quality of life [2,10,11]. It is not associated with other primary or systemic skin diseases, psychological disorders or acute renal failure. The pathogenesis is not fully known, but there is a relation with hyperparathyroidism, xerosis, hypervitaminosis A, iron deficiency anemia, and elevated serum levels of magnesium, calcium, phosphate, aluminum and histamine, though the latter may be associated with allergic sensitization to components in dialysis membranes. Pruritus contributes to the appearance of perforating injuries by the Koebner phenomenon [12-16].

Moreover, there is no relationship between the plasma level of PTH and dermal Cell proliferation, nor is there a difference in the number of mast cells or the levels of PTH between patients with or without pruritus.

The pathophysiology of pruritus is multifactorial. Until now, studies reported significant association between serum parathyroid hormone (PTH) and the itching; some other studies have found no specific relationship between pruritus and hyperparathyroidism, hypercalcemia, hyperphosphatemia, and level of PTH [5,9,14,23].

## PATIENTS AND METHODS

This cross-sectional study was conducted on sixty and two patients with ESRD (age ranging from 31 to 87 years) free from systemic, skin or psychiatric disorders and other secondary causes attributable to pruritus, undergoing maintenance HD at Fresenius dialysis center, Banja Luka, Bosnia and Herzegovina were evaluated for pruritus and included in a study during period from December, 2013 to May, 2014. Duration of each session was 4 hours.

Those with history of dermatologic disease or chemical exposure were excluded. Patients were asked to report the severity of their pruritus.

Blood samples were taken from all patients for assessment of serum levels of phosphate, PTH, KT/V (index of dialysis dose), parameters at the beginning of the study and six months after.

## Ethics

This study was performed on human subjects; thus, all patients were aware of the presence of the study and they were fully informed about the drug and its side-effects.

## Statistical Analyses

Descriptive data were compared as a mean  $\pm$  standard deviation (range). Mann-Whitney U test and T-test was used to compare means between patients with and without pruritus.

Wilcoxon Signed Rank Test and Chi-square test with Yates correction factor were used for relationship of quantitative data and comparison of qualitative variables respectively. The level of significance was  $p < 0.05$ .

## RESULTS

The overall prevalence of pruritus in the present study is 45,2%.

Pruritus has been discovered in 21 out of 34 males (54,8%) and 6 out of 28 females (22,2%).

Applying  $\chi^2$  test with Yates correction was highly statistically significant ( $\chi^2 = 8.003$ ,  $p = 0.005$ ) by gender. Analysis of the gender revealed that pruritus was significantly more detected in men, as shown in Table 1.

According to patients' age no significant differences were found (applying T-Test (Independent Samples),  $t = -0.443$ ,  $p = 0.659$ ).

Applying the Mann-Whitney-U test, there was no statistically significant difference in the duration HD/months/by groups of patients with pruritus ( $n = 27$ ,  $Md = 84.00$ ) and those without pruritus ( $n = 35$ ,

**Table 1:** Pruritus in relation to patients' gender

Gender of the patients	Patients		Total
	Patients with pruritus	Patients without pruritus	
Male			
N	21	13	34
%	77.8	37.1	54.8
Female			
N	6	22	28
%	22.2	62.9	45.2
Total			
N	27	35	62
%	100.0	100.0	100.0

Md = 75.00),  $U = 421.00$ ,  $z = -0.731$ ,  $p = 0.465$ ,  $r = 0.092$  (Table 2).

Using the Mann-Whitney-U test, there was no statistically significant difference in KTVI by groups of patients with pruritus ( $n = 27$ , Md = 1.56) and patients without pruritus ( $n = 35$ , Md = 1.65),  $U = 339.50$ ,  $z = -1.889$ ,  $p = 0.059$ ,  $r = 0.239$ , the laboratory determined the start of the study as shown in Table 3.

Using the T-test for independent samples there was no statistically significant difference ( $t = -1.166$ ,  $p = 0.248$ ) in KT/V2 examined groups of subjects, measured at the end of the study.

Using the Mann-Whitney-U test, there was no statistically significant difference of level Phosphate 1 in serum by groups of patients with pruritus ( $N = 27$ , Md = 1.42) and patients without pruritus ( $N = 35$ , Md = 1.33),  $U = 371.50$ ,  $z = -1.434$ ,  $p = 0.151$ ,  $r = 0.182$ . The laboratory determined the start of the study as shown in Table 4.

Using the Mann-Whitney-U, test there was no statistically significant difference of level Phosphate 1 in serum by groups of patients with pruritus ( $N = 27$ , Md = 1.26) and patients without pruritus ( $N = 35$ , Md = 1.30),  $U = 456.50$ ,  $z = -0.227$ ,  $p = 0.820$ ,  $r = 0.029$ , measured at the end of the study.

Using the Mann-Whitney-U test, there was no statistically significant difference in PTH 1 by groups of patients with

**Table 2:** HD duration (months)

Group	N	Min.	Max.	Range	Median	Mean	Std. Dev.
Patients with pruritus	27	19	348	329	84.00	89.33	63.901
Patients without pruritus	35	4	299	295	75.00	85.14	70.801
Total	62	4	348	344	79.50	86.97	67.371

**Table 3:** Comparison of values KT/V 1 (index of dialysis dose)

Group	N	Min.	Max.	Range	Median	Mean	Std. Dev.
Patients with pruritus	27	1.24	1.99	0.75	1.5600	1.5552	0.19964
Patients without pruritus	35	1.28	2.44	1.16	1.6500	1.6820	0.25395
Total	62	1.24	2.44	1.20	1.6000	1.6268	0.23865

**Table 4:** Comparison of Phosphate 1 level in serum

Group	N	Min.	Max.	Range	Median	Mean	Std. dev.
Patients with pruritus	27	0.53	3.27	2.74	1.4200	1.4370	0.48337
Patients without pruritus	35	0.69	2.37	1.68	1.3300	1.2889	0.31249
Total	62	0.53	3.27	2.74	1.3400	1.3534	0.39938

pruritus ( $N = 27$ , Md = 194.50) and patients without pruritus ( $N = 35$ , Md = 245.80),  $U = 453.00$ ,  $z = -0.277$ ,  $p = 0.782$ ,  $r = 0.035$  as shown in Table 5.

Using the Mann-Whitney-U test, there was no statistically significant difference in PTH 2 by groups of patients with pruritus ( $N = 27$ , Md = 218.20) and patients without pruritus ( $N = 35$ , Md = 214.70),  $U = 455.00$ ,  $z = -0.248$ ,  $p = 0.804$ ,  $r = 0.031$ .

By applying the Wilcoxon test of paired couples there was no statistically significant difference in patients with pruritus neither in the change of KT/V2 and KT/V1 ( $z = 0.000$ ,  $p = 1.000$ ), nor in the change of Phosphates2 and Phosphates ( $z = -1.261$ ,  $p = 0.207$ ) nor in the change of PTH2 and PTH2 ( $z = -0.505$ ,  $p = 0.614$ ), that is the measured laboratory value at the beginning of the study as shown in Table 6.

By applying the Wilcoxon test of paired couples there was no statistically significant difference in patients without pruritus neither in the change of KT/V2 and KT/V1 ( $z = -1.720$ ,  $p = 0.085$ ), nor in the change of Phosphates2 and Phosphates ( $z = -0.377$ ,  $p = 0.706$ ), nor in the change of PTH2 and PTH2 ( $z = -0.419$ ,  $p = 0.675$ ), measured at the end of the study as shown in Table 7.

## DISCUSSION

We conducted the first study of uremic pruritus in Republic of Srpska (Bosnia and Herzegovina).

**Table 5:** Comparison of PTH 1 level in serum

Group	N	Min.	Max.	Range	Median	Mean	Std. Dev.
Patients with pruritus	27	31.1	1885.0	1853.9	194.500	355.287	437.6542
Patients without pruritus	35	30.7	2150.0	2119.3	245.800	335.447	388.8529
Total	62	30.7	2150.0	2119.3	197.150	344.087	407.4530

**Table 6:** Comparisons within groups

Patients with pruritus	KT/V 2 – KT/V 1	Phosphate2 - Phosphate1	PTH 2 - PTH 1
z	0.000 <sup>b</sup>	-1.261 <sup>c</sup>	-0.505 <sup>c</sup>
p	1.000	0.207	0.614

<sup>a</sup>Wilcoxon Signed Ranks Test, <sup>b</sup>The sum of negative ranks equals the sum of positive ranks, <sup>c</sup>Based on positive ranks

**Table 7:** Comparisons within groups

Patients without pruritus	KT/V 2 – KT/V 1	Phosphate2 - Phosphate1	PTH 2 - PTH 1
z	-1.720 <sup>b</sup>	-0.377 <sup>c</sup>	-0.419 <sup>b</sup>
p	0.085	0.706	0.675

<sup>a</sup>Wilcoxon Signed Ranks Test, <sup>b</sup>Based on positive ranks, <sup>c</sup>Based on negative ranks

Our study as many others showed that pruritus is very common (45.2%) in HD patients.

The overall prevalence of pruritus among our study population is 45,2 % and it is comparable with the published reports [1,3-5,14,17-19,20-22,24].

Pruritus has been detected in 21 out of 34 males (54,8%) and 6 out of 28 females (22,2%).

Analysis of the gender revealed that pruritus was significantly more shown in men, and previous studies have shown no difference in gender [24].

Men in the DOPPS I and I Studies had UP more often than women. In contrast, Snit M. et al. report that UP occurred statistically significantly more often in women, independent of method of renal replacement therapy [1,14].

In our study, we did not find any relationship between pruritus and duration of dialysis as seen in some previous studies [14,21,23,24].

Like most of other studies, we could not find any relationship between serum levels of phosphorus and UP in the patients' [24].

Hyperparathyroidism has been proposed by some authors as a cause of uremic pruritus [24]. Hyperparathyroidism can stimulate mast cells to release histamine and can promote microprecipitation of calcium and magnesium salts in the skin. On the other hand, all of the patients with severe hyperparathyroidism do not have pruritus. Moreover, there is no relationship between the plasma level of PTH and proliferation of dermal cell, and there is no difference in the number of mast cells and the levels of PTH between patients with or without pruritus. On the other hand, a direct role for parathyroid hormone as a cause of uremic pruritus has been questioned because of the failure of intradermal injections of PTH analogs to produce pruritus, and because of negative immunohistochemical studies for PTH in the skin biopsy specimens [24].

Furthermore, no correlation between PTH levels and itching intensity was found in most studies [14,21,23].

In our study, we did not find any relationship between pruritus and the plasma level of PTH.

## CONCLUSIONS

This first cross-sectional study describes key features

UP in Republic of Srpska and results that the UP is significantly more common in men.

This study demonstrates that the serum level of PTH and phosphate isn't associated with the incidence of pruritus in HD patients.

## Statement of Human and Animal Rights

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

## Statement of Informed Consent

Informed consent was obtained from all patients for being included in the study.

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