

# Factors Associated with Uremic Pruritus in Patients Undergoing Hemodialysis: A report from Arak Valiasr Hospital

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## Introduction

Pruritus is a common irritating symptom in patients suffering from chronic renal failure<sup>1,2</sup>. In a study from Nepal, pruritus was more common in patients with end stage renal disease (ESRD) who were being treated by hemodialysis than those who were not receiving hemodialysis<sup>3</sup>. In most of the studies, pruritus has been seen in 41.9% to 67% of ESRD patients receiving hemodialysis<sup>2,4,5</sup>.

In this group of patients, pruritus is extremely disabling<sup>1</sup> and has a lot of negative effects on their quality of life<sup>6</sup>. Pathogenesis of pruritus in these patients is not clearly established<sup>7,8</sup>. Increased levels of calcium, phosphate, parathormon hormone (PTH), Vitamin A hypervitaminosis, skin dryness, biliary acids, nitric

oxide, neurologic changes, substances released by mast cells (histamine, IL-2, proteases, substance P) are important factors that have been proposed as offensive agents in uremic pruritus<sup>2,6</sup>.

The prevalence and pattern of pruritus in hemodialysis patients vary in different studies. In some studies, pruritus was seen more in females<sup>9</sup>; however, in most other studies, no difference was seen between men and women<sup>4</sup>. In some of the reports, pruritus had a higher prevalence and severity among older patients<sup>10,11</sup> but in other reports, there was no difference in the prevalence and severity at different ages<sup>9</sup>.

In most studies, pruritus was seen more in patients being hemodialysed for longer periods of time<sup>10,12</sup>, while in some reports, this difference was not

## Abstract

**Background:** Pruritus is one of the most disabling problems in patients with chronic renal failure. It is a distressing symptom with a negative impact on quality of life and is also very frustrating for both patients and their physicians. The pathophysiological mechanisms of pruritus are mainly unknown. The aim of this study was to identify factors associated with pruritus in these patients.

**Methods:** This cross sectional study was done on 100 patients who were under hemodialysis because of end stage renal disease. In patients who were suffering from uremic pruritus, the severity of pruritus was assessed and the relationship between the presence and severity of pruritus with serum levels of hemoglobin, creatinine, urea, phosphate, calcium, albumin, parathormone hormone (PTH) and alkaline phosphatase was evaluated.

**Results:** One hundred patients (48 women and 52 men) entered this study. Pruritus was found in 45% of the patients. We found a significant relationship between severity of pruritus with age and serum level of phosphate. No significant correlation was found between the severity of pruritus and sex, duration of dialysis, underlying renal disease and serum levels of hemoglobin, urea, albumin, PTH, alkaline phosphatase, calcium, and creatinine.

**Conclusions:** Pruritus is still a common problem in hemodialysis – dependent patients. Higher serum levels of phosphate seems to be an important factor associated with uremic pruritus. (*Iran J Dermatol 2010;13: 12-15*)

**Key words:** pruritus, uremic pruritus, end-stage renal disease, renal failure, hemodialysis, phosphate

approved and no relationship was seen between pruritus and the duration of hemodialysis<sup>10,13</sup>. In some studies, pruritus was more common in patients with higher levels of serum calcium<sup>12,14</sup> and phosphate<sup>6</sup>. However, in most of the other reports, no linkage was found between laboratory parameters such as serum calcium, phosphate, PTH, hemoglobin, alkaline phosphatase, albumin, urea, creatinine and pruritus<sup>10,13,15</sup>.

Regarding the controversial results of these studies, we decided to assess the association of these laboratory factors with pruritus in patients who were receiving hemodialysis in hemodialysis center of Arak Valiasr hospital.

## Patients and Methods

### Patients

This cross sectional study was done on 100 patients who were under hemodialysis because of end stage renal disease at the hemodialysis unit of Valiasr hospital. This study was performed in accordance with the declaration of Helsinki and was approved by Arak Medical University Ethics Committee. Volunteer patients entered the study. All patients were hemodialysed for 4 hours 3 times a week. The membrane which was used for hemodialysis was from polysulfane and the salt was mostly sodium acetate and hypochloride. Patients with underlying skin diseases, psychological disorders or any other secondary causes of pruritus were excluded. All patients were tested for serum levels of calcium, phosphate, PTH, hemoglobin, alkaline phosphatase, albumin, urea, and creatinine. At the same time, patients were asked whether they had pruritus or not.

### Pruritus assessment

Severity of pruritus was assessed by a method based on the one proposed by Duo<sup>16</sup> and modified by Mettang et al<sup>17,18</sup>. The score was assessed by the same investigator for all patients. This method was based on criteria including scratching, severity, frequency and distribution of pruritus, and pruritus-related sleep disturbance as follows:

**Scratching:** For pruritus in each reported period of time (morning: the time from getting up until noon, afternoon: the time from noon until going to bed and night), 1 point was allocated with a maximum of 3 points.

**Severity:** A slight itching sensation without necessity for scratching received 1 point, a few times of scratching received 2 points, frequent

scratching received 3 points, and scratching without relief of pruritus received 4 points. Pruritus causing total restlessness received 5 points.

**Distribution:** Each location (arms, legs or trunk) received 1 point and if generalized pruritus was present, 5 points was given.

**Frequency:** It was evaluated by the number of pruritus episodes and their duration. Every two short episodes (< 10 min) or one long episode (>= 10 min) received 1 point, with a maximum of 5 points for ten or more short episodes or for five or more long episodes.

**Sleep Disturbance:** Patients were asked to write down the number of sleeping hours and the frequency of arousal from sleep during the night because of itching. Absence of sleep received 10 points and seven or more hours of sleeping received 0. Other points could be scored by the deduction of the number of sleeping hours from 10.

For severity, distribution and frequency, separate scores were recorded for morning and afternoon. Thus the highest possible score for a 24-hour period was 48 points.

Patients with a severity score (SS) of 1-16, 17-32 and 33-48 were placed in the group of mild pruritus, moderate pruritus and severe pruritus, respectively.

Data were analyzed by SPSS software and t-test, U-Mann-Whitney, ANOVA and Pierson tests.

## Results

From 100 patients who entered the study, 48% were women and 52% were men. Mean age of the patients was 59.9 years (range: 23-86 years) with the prevalence being highest between 50 and 70 years of age. The most prevalent cause of renal failure was hypertension (37%) followed by diabetes mellitus, glomerulonephritis, polycystic kidney and urological problems. In 18% of the cases, the cause of renal failure was unknown. About 45% of the patients were suffering from pruritus (55.6% had mild pruritus, 33.3% had moderate pruritus and 11.1% had severe pruritus).

The average of SS was  $8.35 \pm 10.74$  in men and  $5.44 \pm 13.91$  in women. U-Mann-Whitney and t-test showed no significant difference between genders in the mean severity of pruritus. Mean SS in patients under 70 years of age was  $6.79 \pm 10.75$ . On the other hand, mean SS in patients who were 70 years or older was  $12.31 \pm 14.96$ . A statistically significant difference was found between these two groups (table 1). In other words,

**Table1.** Pruritus score according to age in hemodialysis patients

Age	Minimum of pruritus score	Maximum of pruritus score	Mean of pruritus score± standard deviation
<50 years	0	48	6.6 ± 12.1
50-70 years	0	38	6.8 ± 10
>50 years	0	48	12.31 ± 14.9

**Table2.** Pruritus score according to the underlying renal disease in hemodialysis patients

Underlying disease	Minimum of pruritus score	Maximum of pruritus score	Mean of pruritus score± standard deviation
Hypertension	0	48	8.27 ± 13.9
Polycystic kidney	0	31	9.28 ± 14.2
Glomeronephritis	0	13	2.6 ± 5.8
Urologic problem	5	13	9 ± 5.6
Diabetes	0	37	9.3 ± 11.3
Unknown	0	29	6.7 ± 10.2

**Table3.** Pruritus score according to duration of dialysis in patients with end stage renal disease

Duration of dialysis	Minimum of pruritus score	Maximum of pruritus score	Mean of pruritus score± standard deviation
<1 year	0	29	7.9 ± 9.8
1-5 years	0	48	9.4 ± 12.9
>5 years	0	48	6.6 ± 12.5

patients who were 70 years or older experienced more severe pruritus than younger patients. Variance analysis test was used to compare average severity score of pruritus in different underlying renal disorders groups (table 2). No significant relation was found between average score of pruritus and underlying kidney disorders.

There was no relation between average severity of pruritus and duration of hemodialysis (table 3). Although there was no significant relation between calcium, PTH, hemoglobin, alkaline phosphatase, albumin, urea, creatinine levels and pruritus, there was a direct relation between serum phosphate level and pruritus ( $P=0.04$ ).

## Discussion

Szepietowski et al. studied 50 patients treated by hemodialysis and found pruritus in 40.8% of them<sup>9</sup>, which was comparable to 45% in our study. In a study by Wikstrom et al, pruritus was present in 46% of the patients<sup>6</sup>, and in a similar study from Iran, Akhyani et al, reported pruritus in 41.9% of 167 patients who underwent hemodialysis<sup>13</sup>.

In this study, pruritus was more severe in patients older than seventy years old. In a study by Jamal et al, sub-group analysis with reference to age and sex revealed that pruritus was significantly more in women aged 45 years and older when compared to men of similar age-group or women below 45

years<sup>11</sup>. Most other studies found no relationship between age and the severity of pruritus. However, it should be mentioned that the relationship established in our study might be due to more skin xerosis in older patients. In the present study, the average scale of pruritus was higher in women but t-test showed no statistically significant difference between genders, similar to the results of most other studies<sup>13-15</sup>. However, Szepietowski et al, reported that itching was more common in female patients<sup>6</sup>. We found no relationship between the underlying kidney disease and pruritus. A similar result has been reported by many investigators including Duque et al,<sup>12</sup> and Mesic et al<sup>10</sup>.

We found a significant relationship between pruritus and serum levels of phosphate, but not calcium, in our patients. Narita et al, reported both hypercalcemia and hyperphosphatemia as independent risk factors for the development of severe pruritus<sup>14</sup>. Also, Wikstrom et al, observed a direct relationship between pruritus and calcium, phosphorous level<sup>6</sup>. However, Duque et al, reported a correlation only between serum calcium concentration and pruritus<sup>12</sup>.

We did not find any relationship between pruritus and the levels of blood urea, hemoglobin, serum albumin, PTH, alkaline phosphatase, and creatinin. Similar results were reported by Dyachenko et al,<sup>4</sup> and Akhyani et al<sup>13</sup>.

The results of the present study provide support for the possible involvement of phosphate metabolism in the development of pruritus in end-stage renal disease patients who are receiving hemodialysis. Further delineation of factors that affect the severity of uremic pruritus or may have a role in its development can provide promises for future management of pruritus and improvement of patients' quality of life.

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