

# PRURITUS IN HEMODIALYSIS PATIENTS : RELATION TO SERUM UREA, PARATHORMONE, AND HISTAMINE LEVELS

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## SUMMARY :

**Purpose :** Our aim was to investigate the roles of the levels of serum urea, parathyroid hormone and plasma histamine on the pathogenesis of hemodialysis pruritus. **Methods :** Levels of plasma histamine, urea and parathyroid hormone in 40 patients with pruritus and 20 healthy controls were determined. **Results :** The levels of plasma histamine, urea, parathyroid hormone in study group were significantly higher than those of the controls ( $p < 0.01$  for all comparisons). There were no correlations between itch score and plasma histamine, parathyroid hormone, or urea. **Conclusion :** We conclude that the etiology of pruritus in hemodialysis patients is not related to the increased levels of plasma histamine, urea and parathyroid hormone, and requires further investigation.

**Key Words:** Pruritus, Hemodialysis, Urea, Parathyroid Hormon, Histamine.

## INTRODUCTION

Generalized pruritus is one of the most common features of chronic renal failure (1, 2, 3). Pruritus in patients undergoing dialysis treatment was first reported in 1932. The prevalence of pruritus was reported to be 13 % (4). Later, the prevalence figure has been reported to be in the range of 15 % to 90 % (1, 5, 6, 7). Hemodialysis is suggested to be an important trigger of pruritus. The pruritus can be intermittent and mild, or it can be continuous and severe (8, 9). Several studies have been conducted to examine the relationship between pruritus and the duration and number of hemodialysis sessions. Although there are studies reporting that pruritus decreases or is eliminated with hemodialysis, other studies report the opposite effect (4, 6, 8).

Although the pathogenesis of the hemodialysis

pruritus is unclear, various factors are hold responsible. In this study, we investigated the roles of the levels of serum urea, parathyroid hormone and plasma histamine on the pathogenesis of hemodialysis pruritus. In addition, we questioned the existence of a correlation between the severity of pruritus and the levels of serum urea, parathyroid hormone and plasma histamine.

## MATERIAL AND METHODS

Forty (22 male, 18 female) hemodialysis patients with pruritus in Isparta State Hospital Hemodialysis Unit were included in the study. The control group consisted of 20 healthy persons (10 males, 10 females). The patients were examined dermatologically and the characteristics of pruritus were recorded. The severity of pruritus was graded between 0 and 5 as follows :

- Grade 0 : No pruritus
- Grade 1 : Occasional mild pruritus
- Grade 2 : Continuous mild pruritus
- Grade 3 : Medium pruritus
- Grade 4 : Severe pruritus that affects resting but not activity
- Grade 5 : Severe pruritus that affects both resting and activity

The serum samples of the control group and the patients obtained before hemodialysis were stored at -20°C until worked on. Serum urea, creatinine, parathormone, and histamine levels of the hemodialysis group were measured. In the control group, serum urea, parathormone, and histamine levels were measured. Serum urea, parathormone, and histamine levels of the two groups were compared. Furthermore, the correlation between pruritus severity and the levels of serum urea, parathormone, and histamine was investigated. Student-t test has been used for statistical analyses.

### RESULTS

The mean age of the hemodialysis group was 49.92 years (range 13 to 72 years). The mean hemodialysis duration was 18.25 months (range 2 months to 4 years). Table 1 depicts the dermatological examination results of the hemodialysis group. Pruritus increased in 27.5 % of the patients, whereas it decreased in 22.5 % and remained the same in 50 % of the patients. The pruritus severity grades were evaluated to be grade 1, 2, 3, 4, and 5 in 7.5 %, 27.5 %, 42.5 %, 12.5 %, and 10 % of the patients, respectively.

Serum urea levels were high in all of the hemodialysis patients; the mean level was  $277.12 \pm 0.95$  mg/dl (range 49 to 359). There was no correlation between pruritus severity and the serum urea levels. In the control group, the serum urea levels were within normal levels.

The mean serum parathormone level was  $331.14 \pm 3.74$  pg/ml (range 7.4 to 632) in the hemodialysis group. In the control group, the mean value was  $34.49 \pm 0.56$  pg/ml (range 7.8 to 58.1). Serum parathormone level was significantly higher in the hemodialysis group compared to the control group ( $p < 0.01$ ) (Fig. 1). There was no correlation between the severity of pruritus and the serum parathormone level in the hemodialysis group (Fig. 2).

	n	%
Pruritus	40	100.0
Xerosis	19	47.5
Concave nail deformity	9	22.5
Tinea pedis	7	17.5
Exaggerated longitudinal ridging	6	15.0
Hyperpigmentation	5	12.5
Nail pitting	4	10.0
Punctate erosion	4	10.0
Tinea unguium	4	10.0
Petechiae-Ecchymoses	4	10.0
Onycholysis	4	10.0
Keratosis pilaris	3	7.5
Alopecia	3	7.5
Vitiligo	2	5.0
Leukonychia	2	5.0
Splinter hemorrhages	2	5.0

Table 1 : The dermatological examination results of the patients.

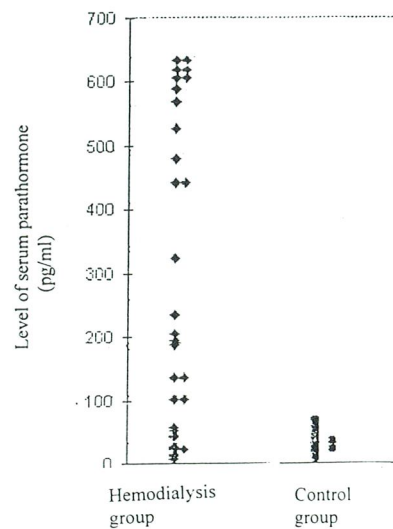


Fig 1 : Serum parathormone levels in the hemodialysis and control groups.

The mean serum histamine level was  $2.87 \pm 1.69$  nmol/l (range 0.33 to 16.0). The mean value in the control group was  $0.82 \pm 0.25$  nmol/l (range 0.32 to 1.12). The serum histamine level was significantly higher in the hemodialysis group compared to the control group ( $p < 0.01$ ) (Fig. 3). There was no correlation between the severity of pruritus and serum histamine level in the hemodialysis group (Fig. 4).



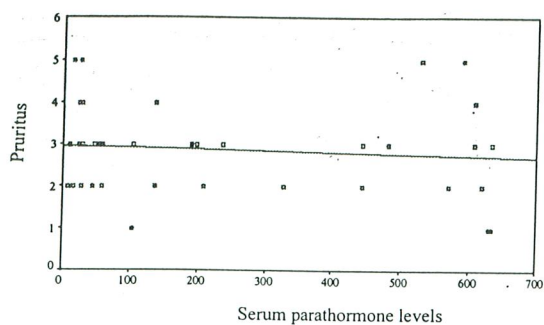


Fig 2 : Comparison of the severity of pruritus and serum parathormone level.

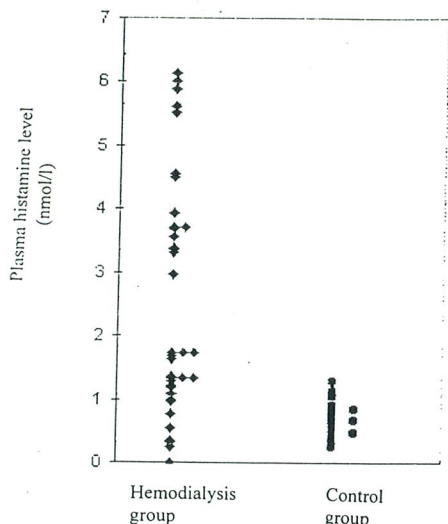


Fig 3 : Plasma histamine levels in the hemodialysis and control groups.

## DISCUSSION

The etiology of pruritus in hemodialysis patients remains unknown. Various factors, such as high serum vitamin A levels, hypermagnesemia, hyperphosphatemia, hypercalcemia, or drugs used in chronic renal failure have been suggested to cause pruritus in patients undergoing hemodialysis (3, 6, 10-14). In addition to these factors, high serum urea levels, secondary hyperparathyroidism, or high plasma histamine levels have been suggested in the etiopathogenesis of the pruritus.

Conflicting studies have been reported on the relation between pruritus and high serum urea le-

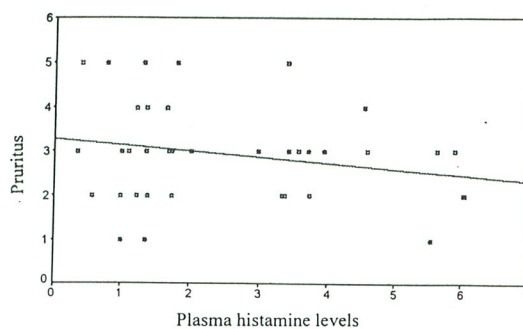


Fig 4 : Comparison of the prurits severity and plasma histamine level.

vels. However, high serum urea level is not considered to be the major responsible factor for pruritus (4, 10, 15). In several studies, it has been reported that no correlation exists between high levels of serum calcium, phosphate, magnesium, alkaline phosphatase, creatinine and pruritus (4, 15, 16).

In our study, serum urea levels were high in all of the patients; however, there was no correlation between the high serum urea level and the severity of pruritus. In addition, pruritus has increased in 27.5 % of the patients; thus, we think that high serum urea level is not the major responsible factor for pruritus.

Secondary hyperparathyroidism is frequently observed in hemodialysis patients (6, 17). In some studies, parathormone levels were reported to be higher in pruritic hemodialysis patients compared to nonpruritic hemodialysis patients. In addition, pruritus was reported to be eliminated in a short period following parathyroidectomy. These results indicate that secondary hyperparathyroidism may be a major factor for pruritus (6, 15, 18). Some researchers suggested that secondary hyperparathyroidism causes histamine to be released from mast cells (6, 15, 16, 18). On the other hand, there are studies reporting the opposite view (4, 5, 6, 17, 19).

In our study, the parathormone level was significantly higher in the hemodialysis group compared to the control group ( $p < 0.01$ ). There was no correlation between the parathormone level and the severity of pruritus. These results suggest that secondary hyperparathyroidism is not a major factor for

pruritus in hemodialysis patients.

Increase in plasma histamine levels is another possible factor in the etiopathogenesis of the hemodialysis pruritus. Researchers suggested that the increase in plasma histamine level may be caused by an augmented number of mast cells, various membranes used for dialysis, sterilisation methods, or accumulated histamine which is normally excreted by the kidney (5, 12, 16, 20-25).

In our study, the plasma histamine level was significantly higher in the hemodialysis group compared to the control group ( $p<0.01$ ). There was no correlation between the plasma histamine levels and the severity of pruritus.

In this study, we have examined the levels of serum urea, parathormone and plasma histamine that are held responsible in the etiopathogenesis of the hemodialysis pruritus. Although all three factors were higher in the hemodialysis group compared to the control group, there were no correlations between these levels and the severity of pruritus. We think that the etiopathogenesis of the hemodialysis pruritus is rather complex and further studies should be conducted to clarify the etiopathogenesis of the pruritus.

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