



Clinical, Biochemical and Dialysis Adequacy Markers Associated with Chronic Kidney Disease-Associated Pruritus among Hemodialysis Patients: A Retrospective Observational Study

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ABSTRACT:

Background: Chronic kidney disease-associated pruritus (CKD-aP) is a frequent and distressing symptom among patients receiving maintenance hemodialysis. In routine practice, evaluation often depends on readily available biochemical and dialysis adequacy parameters rather than non-routine assays. **Objectives:** To estimate the documented prevalence of CKD-aP among maintenance hemodialysis patients and to examine its association with routine markers including intact parathyroid hormone (iPTH), corrected calcium, serum phosphate, kidney function test parameters, complete blood count, alkaline phosphatase, single-pool Kt/V and hemodialysis frequency. **Methods:** This hospital-based retrospective observational study reviewed records of adult maintenance hemodialysis patients treated at a tertiary care center in Delhi. Patients receiving hemodialysis for at least 3 months with available routine biochemical, hematological and dialysis adequacy data were included. CKD-aP status and severity were abstracted from hemodialysis and dermatology notes. The routine markers analyzed were iPTH, corrected calcium, phosphate, pre-dialysis urea, serum creatinine, hemoglobin, total leukocyte count, platelet count, alkaline phosphatase, single-pool Kt/V and hemodialysis frequency. Between-group comparisons, severity-stratified analyses, correlation testing and multivariable logistic regression were performed. **Results:** Among 120 eligible hemodialysis records, CKD-aP was documented in 67 patients (55.8%). Patients with CKD-aP had lower single-pool Kt/V, higher serum phosphate, higher iPTH and higher alkaline phosphatase than patients without CKD-aP. Corrected calcium, serum creatinine and complete blood count parameters showed weaker or non-significant group differences. In adjusted analysis, hyperphosphatemia, iPTH >300 pg/mL, alkaline phosphatase >150 IU/L and Kt/V <1.20 were independently associated with CKD-aP. Severity-stratified analysis showed a graded increase in phosphate, iPTH, alkaline phosphatase and composite abnormality burden with worsening

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pruritus. **Conclusion:** CKD-aP among hemodialysis patients was associated mainly with routine markers of mineral-bone disturbance and dialysis adequacy. A retrospective record-based marker panel using phosphate, iPTH, alkaline phosphatase, Kt/V and hemodialysis frequency can support practical screening and clinical prioritization in hemodialysis units.

1. INTRODUCTION:

Chronic kidney disease-associated pruritus (CKD-aP), previously termed uremic pruritus, is a chronic itch occurring in patients with CKD or kidney failure after exclusion of a primary dermatological, hepatobiliary, endocrine, infectious or drug-related cause. It remains one of the most burdensome non-traditional complications of dialysis, with effects on sleep, quality of life, emotional well-being, treatment satisfaction and possibly survival.¹⁻⁴

Indian hemodialysis populations require focused study because dialysis delivery patterns, affordability, frequency of hemodialysis, control of CKD-mineral bone disorder, nutritional status, skin phenotype, climate-related xerosis and access to dermatological care differ from high-income settings. Recent Indian hemodialysis data reported CKD-aP in more than half of maintenance hemodialysis patients and showed deterioration in quality of life and sleep with increasing severity.⁵ Older Indian dermatology-nephrology studies also consistently identify xerosis and pruritus among the most frequent cutaneous manifestations in chronic kidney disease and dialysis.⁶⁻¹⁰

The pathophysiology of CKD-aP is multifactorial. Proposed mechanisms include xerosis, epidermal barrier dysfunction, hyperphosphatemia, secondary hyperparathyroidism, increased calcium-phosphate burden, uremic toxin accumulation, inadequate dialysis clearance, peripheral neuropathy, central sensitization, mast-cell activation and dysregulated opioid receptor signaling.¹¹⁻¹⁶ For a retrospective record-based study, the most reliable and reproducible markers are those routinely captured in hemodialysis records and laboratory systems.

Therefore, the present manuscript was revised as a retrospective observational study using only routinely available markers: intact parathyroid hormone (iPTH), corrected calcium, serum phosphate, kidney function test parameters, complete blood count, alkaline phosphatase, single-pool Kt/V and hemodialysis frequency. This design is suitable for hospital record review, avoids non-routine testing and produces findings that can be translated directly into hemodialysis-unit quality improvement.

MATERIALS AND METHODS

Study design and setting

This was a hospital-based retrospective observational study conducted in the maintenance hemodialysis unit of a tertiary care center in Delhi, India. Existing dialysis-unit records, laboratory records and dermatology/nephrology notes were reviewed for the defined study period. The manuscript was prepared in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) framework.

Study population

Records of adult patients aged 18 years or above receiving maintenance hemodialysis for at least 3 months were screened. Patients were eligible if CKD-aP status was documented and if routine laboratory and dialysis adequacy data were available within the predefined review window. Records were excluded if there was documented active eczema, psoriasis, scabies, urticaria, cholestatic liver disease, uncontrolled thyroid disease, hematological malignancy, active systemic infection, recent systemic corticosteroid or immunobiological therapy, dialysis duration below 3 months, or incomplete marker data.

Operational definition of CKD-aP

CKD-aP was defined from clinical documentation as recurrent or persistent itch occurring in a patient with CKD or kidney failure without a primary dermatological or systemic non-renal cause. Severity was abstracted from available clinical records and grouped as mild, moderate or severe based on the documented clinical assessment or recorded itch numerical rating score when available.^{13,19}

Markers and variables extracted

The marker panel was restricted to tests and dialysis parameters routinely available in patient records: intact parathyroid hormone (iPTH), corrected calcium, serum phosphate, kidney function test parameters including pre-dialysis urea and serum creatinine, complete blood count including hemoglobin, total leukocyte count and platelet

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count, alkaline phosphatase, single-pool Kt/V and hemodialysis frequency. Demographic and hemodialysis descriptors including age, sex and dialysis vintage were extracted only for clinical description and adjustment.

For patients with CKD-aP, the laboratory value closest to the first recorded pruritus assessment during the review period was used. For patients without CKD-aP, the latest eligible dialysis review with complete marker data during the same period was used. Hyperphosphatemia was defined as serum phosphate ≥ 5.5 mg/dL, elevated iPTH as >300 pg/mL, elevated alkaline phosphatase as >150 IU/L, low dialysis adequacy as single-pool Kt/V <1.20 and anemia as hemoglobin <10 g/dL.

Sample size

All eligible records available during the study period were included. A final sample of 120 records was considered adequate for exploratory retrospective analysis and for multivariable modeling with a limited number of prespecified routine markers.

Statistical analysis

Continuous variables were assessed for distribution and expressed as mean $\pm$ standard deviation or median with interquartile range. Categorical variables were summarized as frequency and percentage. Between-group comparisons used Welch t-test, Mann-Whitney U test, chi-square test or Fisher exact test as appropriate. Severity-stratified comparisons used one-way ANOVA, Kruskal-Wallis test or chi-square test. Spearman correlation assessed relationships between routine markers and pruritus severity. Multivariable logistic regression estimated adjusted odds ratios (aORs) for CKD-aP. Statistical significance was set at $p < 0.05$.

RESULTS

Record selection and CKD-aP prevalence

Of 142 hemodialysis records screened, 22 were excluded because of incomplete routine marker data, dialysis duration below 3 months or a documented primary non-renal cause of pruritus. The final analysis included 120 maintenance hemodialysis records. CKD-aP was documented in 67 patients (55.8%), while 53 patients (44.2%) had no documented CKD-aP. Among CKD-aP patients, mild, moderate and severe pruritus were recorded in 31, 29 and 7 patients, respectively (Figure 1).

Baseline, dialysis and routine marker profile

Patients with CKD-aP were older and had lower dialysis adequacy than patients without CKD-aP. Serum phosphate, iPTH and alkaline phosphatase were higher in the CKD-aP group. Corrected calcium, serum creatinine, hemoglobin, total leukocyte count and platelet count did not show significant between-group differences (Table 1).

Table 1. Baseline, dialysis and routine marker profile stratified by CKD-aP status.

Variable	CKD-aP present (n=67)	No CKD-aP (n=53)	p value
Age, years	57.2 $\pm$ 12.7	51.8 $\pm$ 12.0	0.019
Male sex	56 (83.6)	41 (77.4)	0.485
Dialysis vintage, months	30.1 (18.9-44.5)	29.6 (22.1-52.8)	0.552
Twice-weekly hemodialysis	56 (83.6)	37 (69.8)	0.082
Single-pool Kt/V	1.23 $\pm$ 0.18	1.40 $\pm$ 0.21	<0.001
Pre-dialysis urea, mg/dL	145 $\pm$ 34	132 $\pm$ 31	0.032
Serum creatinine, mg/dL	8.6 $\pm$ 2.3	8.2 $\pm$ 2.1	0.330
Corrected calcium, mg/dL	8.6 $\pm$ 0.8	8.7 $\pm$ 0.8	0.839
Serum phosphate, mg/dL	5.7 $\pm$ 1.2	4.9 $\pm$ 1.0	<0.001
iPTH, pg/mL	404 (278-640)	289 (206-473)	0.003
Alkaline phosphatase, IU/L	151 (112-218)	124 (96-178)	0.018
Hemoglobin, g/dL	9.5 $\pm$ 1.4	9.7 $\pm$ 1.4	0.354
Total leukocyte count, $\times 10^3/\mu\text{L}$	7.8 (6.2-9.6)	7.4 (5.9-9.1)	0.441
Platelet count, lakh/ μL	2.15 $\pm$ 0.62	2.23 $\pm$ 0.58	0.468

Values are mean $\pm$ SD, median (IQR), or n (%). p values from Welch t-test, Mann-Whitney U test, chi-square test or Fisher exact test. CKD-aP, chronic kidney disease-associated pruritus; iPTH, intact parathyroid hormone.

Abnormality burden in routine markers

Hyperphosphatemia, elevated iPTH, elevated alkaline phosphatase and low Kt/V were significantly more frequent among patients with CKD-aP. A combined mineral-bone marker abnormality score showed a clear excess burden

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in the CKD-aP group (Table 2).

Table 2. Frequency of abnormal routine markers among patients with and without CKD-aP.

Marker abnormality	CKD-aP present (n=67)	No CKD-aP (n=53)	p value
Hyperphosphatemia: phosphate ≥ 5.5 mg/dL	38 (56.7)	16 (30.2)	0.004
iPTH >300 pg/mL	44 (65.7)	24 (45.3)	0.026
Alkaline phosphatase >150 IU/L	34 (50.7)	15 (28.3)	0.013
Single-pool Kt/V <1.20	30 (44.8)	10 (18.9)	0.003
Twice-weekly hemodialysis	56 (83.6)	37 (69.8)	0.082
Hemoglobin <10 g/dL	44 (65.7)	30 (56.6)	0.304
Total leukocyte count $>11 \times 10^3/\mu\text{L}$	8 (11.9)	4 (7.5)	0.523
Platelet count <1.5 lakh/ μL	10 (14.9)	6 (11.3)	0.594
Corrected calcium abnormality	30 (44.8)	20 (37.7)	0.435
≥ 2 abnormal mineral-bone markers	36 (53.7)	13 (24.5)	0.002

Values are n (%). Corrected calcium abnormality indicates a value below or above the laboratory reference range. Mineral-bone markers included phosphate, iPTH and alkaline phosphatase.

Severity-stratified routine marker pattern

Among patients with CKD-aP, worsening pruritus severity was accompanied by lower Kt/V and progressively higher serum phosphate, iPTH and alkaline phosphatase. The composite count of abnormal routine markers increased across mild, moderate and severe pruritus strata (Table 3).

Table 3. Routine markers among CKD-aP patients by pruritus severity.

Variable	Mild (n=31)	Moderate (n=29)	Severe (n=7)	p value
Patients in severity stratum	31 (46.3)	29 (43.3)	7 (10.4)	-
Single-pool Kt/V	1.31 ± 0.16	1.18 ± 0.15	1.09 ± 0.13	<0.001
Twice-weekly hemodialysis	23 (74.2)	26 (89.7)	7 (100.0)	0.116
Pre-dialysis urea, mg/dL	135 ± 30	150 ± 34	164 ± 37	0.031
Serum creatinine, mg/dL	8.3 ± 2.2	8.9 ± 2.4	9.4 ± 2.6	0.372
Corrected calcium, mg/dL	8.8 ± 0.7	8.5 ± 0.8	8.2 ± 0.9	0.056
Serum phosphate, mg/dL	5.2 ± 1.0	5.9 ± 1.1	6.6 ± 1.3	0.003
iPTH, pg/mL	336 (240-498)	435 (310-682)	690 (510-890)	0.002
Alkaline phosphatase, IU/L	132 (104-192)	167 (123-245)	240 (172-310)	0.006
Hemoglobin, g/dL	9.7 ± 1.2	9.4 ± 1.5	8.8 ± 1.6	0.124
Total leukocyte count, $\times 10^3/\mu\text{L}$	7.4 (6.0-9.1)	8.0 (6.5-9.8)	8.7 (6.7-11.0)	0.309
Platelet count, lakh/ μL	2.22 ± 0.59	2.11 ± 0.66	2.04 ± 0.58	0.721
Composite abnormality count	2 (1-3)	3 (2-4)	4 (3-5)	<0.001

Values are mean $\pm$ SD, median (IQR), or n (%). Severity comparisons used one-way ANOVA, Kruskal-Wallis test or chi-square test as appropriate. Composite abnormality count included abnormal phosphate, iPTH, corrected calcium, alkaline phosphatase, Kt/V and hemoglobin.

Independent routine markers of CKD-aP

In multivariable logistic regression, serum phosphate ≥ 5.5 mg/dL, iPTH >300 pg/mL, alkaline phosphatase >150 IU/L and single-pool Kt/V <1.20 remained independently associated with CKD-aP. Twice-weekly hemodialysis, hemoglobin <10 g/dL and corrected calcium abnormality did not retain independent significance after adjustment. The model c-statistic was 0.78, indicating acceptable discrimination for a routine marker-only retrospective model (Table 4; Figure 2).

Table 4. Multivariable logistic regression and correlation of routine markers with pruritus severity.

Predictor	Adjusted OR (95% CI)	p value	Spearman rho	Correlation p
Serum phosphate ≥ 5.5 mg/dL	3.84 (1.54-9.60)	0.004	0.39	0.001
iPTH >300 pg/mL	2.56 (1.03-6.35)	0.043	0.36	0.003
Alkaline phosphatase >150 IU/L	2.43 (1.01-5.86)	0.048	0.30	0.014
Single-pool Kt/V <1.20	3.12 (1.14-8.50)	0.026	-0.42	<0.001
Twice-weekly hemodialysis	1.89 (0.70-5.08)	0.208	0.22	0.073
Hemoglobin <10 g/dL	1.38 (0.59-3.24)	0.459	-0.18	0.153
Corrected calcium abnormality	1.21 (0.52-2.79)	0.659	-0.11	0.388

Adjusted model included all variables listed in the table with age and sex as adjustment covariates. C-statistic = 0.78; pseudo- $R^2 = 0.28$. Correlations were calculated among CKD-aP patients only. OR, odds ratio; CI, confidence

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interval.

Figures

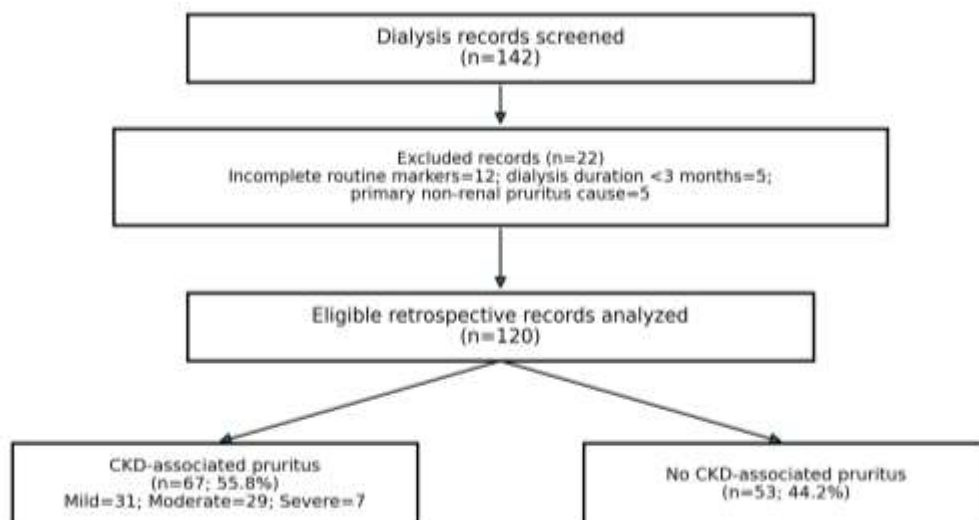


Figure 1. Retrospective record-selection flow and CKD-aP severity distribution.

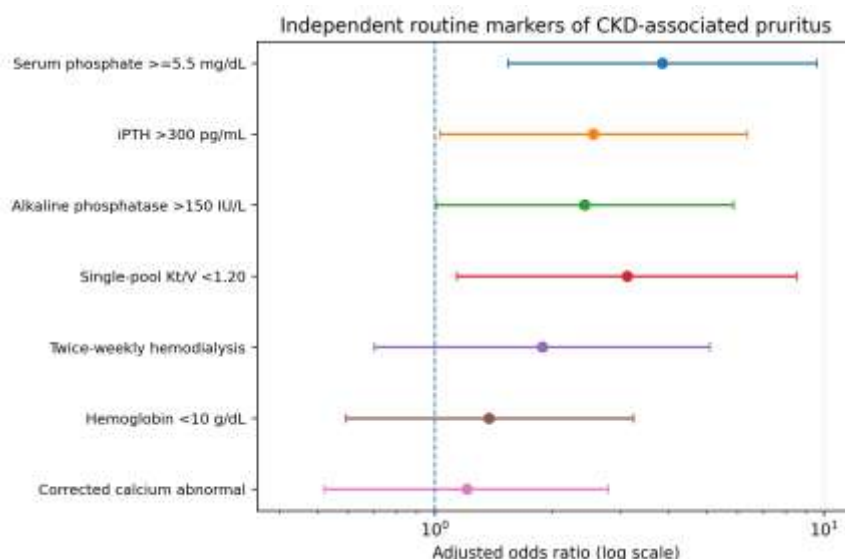


Figure 2. Forest plot of independent routine markers associated with CKD-associated pruritus. Points represent adjusted odds ratios and horizontal bars represent 95% confidence intervals.

DISCUSSION

This retrospective observational study found CKD-aP documented in slightly more than half of maintenance hemodialysis patients, consistent with Indian and global estimates.^{5,6,15,19} By restricting the analysis to routinely available tests and dialysis parameters, the study highlights a practical marker profile that can be implemented in hemodialysis units without specialized biomarker assays.

The strongest routine signals were hyperphosphatemia, elevated iPTH, elevated alkaline phosphatase and low Kt/V. These findings support the continuing relevance of CKD-mineral bone disorder and dialysis adequacy in the clinical work-up of pruritus. The graded rise in phosphate, iPTH and alkaline phosphatase across severity strata suggests that mineral-bone disturbance may contribute not only to the presence of CKD-aP but also to greater symptom burden.

Corrected calcium showed no independent association in this analysis. This may reflect the narrow calcium range typically maintained in dialysis care, the influence of calcium-based binders and vitamin D therapy, and the

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possibility that phosphate, parathyroid hormone and alkaline phosphatase better capture the active mineral-bone phenotype associated with pruritus. Similarly, serum creatinine and routine complete blood count indices were less informative than Kt/V and mineral-bone markers.

Dialysis adequacy remains clinically actionable. A single-pool Kt/V below 1.20 was independently associated with CKD-aP and showed an inverse correlation with severity. Dialysis frequency showed a directionally higher risk but lost independent significance after adjustment, suggesting that delivered adequacy may be more informative than schedule alone. In resource-constrained hemodialysis settings, simultaneous assessment of hemodialysis frequency and Kt/V may help identify patients who require prescription review.

The retrospective design is clinically useful because the required variables are already captured in most hemodialysis units: iPTH, corrected calcium, phosphate, kidney function tests, complete blood count, alkaline phosphatase, Kt/V and hemodialysis frequency. A routine marker-only approach can support screening, follow-up and quality improvement while avoiding dependence on non-routine or research-only assays.

STRENGTHS:

- The study uses a pragmatic retrospective design suitable for routine hospital records.
- The marker panel is limited to tests commonly available in dialysis practice, improving reproducibility.
- The analysis includes both CKD-aP status and severity-stratified marker gradients.
- Multivariable modeling focuses on clinically interpretable and actionable markers.

LIMITATIONS:

- The retrospective design prevents causal inference and depends on the completeness of record documentation.
- CKD-aP may be under-recorded if patients did not spontaneously report itching or if clinicians did not document severity consistently.
- Medication data, phosphate-binder adherence, vitamin D therapy, xerosis treatment, seasonal variation and detailed dermatological grading may not be uniformly available in records.
- The study is single-center and may not represent all Indian hemodialysis settings.
- The laboratory values should be interpreted in relation to dialysis timing and local laboratory reference ranges.

CONCLUSION:

CKD-aP among hemodialysis patients was associated mainly with routine markers of mineral-bone disturbance and dialysis adequacy. Hyperphosphatemia, elevated iPTH, elevated alkaline phosphatase and low Kt/V emerged as the most useful retrospective markers. A routine marker panel using iPTH, corrected calcium, phosphate, kidney function tests, complete blood count, alkaline phosphatase, Kt/V and hemodialysis frequency can support practical screening and prioritization of CKD-aP management in hemodialysis units.

PRACTICE IMPLICATIONS:

1. Screen hemodialysis records and visits for documented CKD-aP rather than relying only on spontaneous patient reporting.
2. Review phosphate, iPTH, alkaline phosphatase and Kt/V in every hemodialysis patient with pruritus.
3. Consider low Kt/V and persistent twice-weekly dialysis as signals for hemodialysis-prescription reassessment.
4. Use CBC and KFT as supportive routine markers, while recognizing that they may be less specific for CKD-aP than phosphate, iPTH, alkaline phosphatase and Kt/V.
5. Create a simple hemodialysis-unit CKD-aP review template that captures pruritus status, severity, hemodialysis frequency, Kt/V and the routine marker panel.

DECLARATIONS:

Availability of data and materials: De-identified study data may be available from the corresponding author on reasonable request, subject to institutional policy.

Competing interests: None declared.

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Authors' contributions: [Author initials] conceptualized the study. [Author initials] extracted data from records. [Author initials] performed statistical analysis. [Author initials] drafted the manuscript. All authors reviewed and

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approved the final manuscript.

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