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ORIGINAL ARTICLE

Incidence of tertiary hyperparathyroidism in CKD patients on hemodialysis.

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ABSTRACT… Objective: This study aimed to determine the incidence of tertiary hyperparathyroidism (THPT) among chronic kidney disease (CKD) patients on long-term hemodialysis in Swat, Pakistan, and identify key risk factors and complications. **Study Design:** Cross-sectional study. **Setting:** Miangul Abdul Haq Jahanzeb Kidney Teaching Hospital, Manglor Swat. **Period:** Jan and Feb 2025. **Methods:** A total of 200 adult hemodialysis patients (≥5 years) were screened. THPT was diagnosed based on persistently elevated parathyroid hormone (PTH) levels (>300 pg/mL), hypercalcemia (>10.5 mg/dL), and phosphate imbalance. Statistical analysis included independent t-tests, Chi-square tests, and binary logistic regression. **Results:** The incidence of THPT was **36% (n=72)**. Significant predictors included dialysis duration >10 years (OR: 2.67; p<0.001), PTH >300 pg/mL (OR: 3.21; p<0.001), hypercalcemia (OR: 2.89; p<0.001), and lack of vitamin D therapy (OR: 1.98; p=0.002). THPT patients exhibited higher rates of vascular calcifications (48% vs. 22%), fractures (12% vs. 3%), and gastrointestinal complications (18% vs. 7%) (p<0.05). **Conclusion:** The high burden of THPT (36%) among hemodialysis patients highlights the need for early screening, vitamin D supplementation, phosphate control, and timely parathyroidectomy referrals to mitigate complications.

Key words: Chronic Kidney Disease, Hemodialysis, Parathyroid Hormone, Tertiary Hyperparathyroidism.

INTRODUCTION

Tertiary hyperparathyroidism (THPT) is frequently seen in patients with chronic kidney disease (CKD) with a long history of hemodialysis due to persisting secondary hyperparathyroidism and hyper stimulated parathyroid glands. Eventually, there is autonomous secretion of parathyroid hormone (PTH) due to parathyroid hypertrophy leading to severe disordered calcium-phosphate metabolism, hypercalcemia, vascular calcification, and osteodystrophy, which dramatically worsens the morbidity and mortality of these patients. In spite of the development of medical treatment options such as vitamin D analogs, calcimimetics, and phosphate binders, a significant proportion of cases of THPT remain unresponsive to pharmacological treatment, making parathyroidectomy the only remaining option. Unfortunately, THPT is underrecognized and as a result undertreated because it is driven by unstandardized diagnostic thresholds, heterogenous treatment approaches, and limited focus on long term follow up care. As hemodialysis patients are at the greatest risk for THPT, knowing its incidence, associated factors, and clinical consequences is essential for effective management and improving patient outcomes.[1] If left untreated, THPT contributes to severe metabolic imbalance, including hypercalcemia, vascular calcification, and cardiovascular diseases all of which significantly increased morbidity and mortality in hemodialysis patients.[2,3]

In chronic kidney disease (CKD) there is already a triad of hypocalcemia, vitamin D deficiency, and phosphate excretion that drives the polyglandular syndrome vis a vis over reacted parathyroid glands.[4] This ultimately progresses into a state of calcium dysregulation PTH deficient secretion leading to what is known as parathyroid hyperplasia.[5]

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This increased para-thyroid glands dysfunction is associated with shift mineral and bone metabolism disorders together with prolonged dialysis which explicitly state the high prevalence THPT in long term dialysis patients.[6] There are different rates of the development of THPT among patients with chronic kidney disease and maintaining dialysis.[7]

Few estimates state that after a decade on dialysis, approximately 15% of the patients would have undergone a parathyroidectomy, while the proportion would be at 38% after twenty years.[7] One meta-analysis suggested that around 20-30% of dialysis patients suffer from THPT and this condition significantly impairs their bone health, cardiovascular system and life expectancy.[8] Because of such high prevalence among patients on hemodialysis, it is crucial to understand the risk factors associated with THPT to improve patient management. Noteworthy THPT risk factors include extended periods of dialysis, hyperparathyroidism with PTH levels persistently elevated above 300 pg/mL, calcimimetic treatments, and SHPT mismanagement during dialysis procedures.[9] Other than bone metabolism, THPT is believed to have widespread consequences affecting multiple organ systems.

Patients on hemodialysis with THPT are more susceptible to vascular calcifications which further escalate cardiovascular disease and mortality.[10] At the same time, permitting hypercalcemia for prolonged periods causes soft tissue calcification, bone nephrolithiasis, and even pancreatitis, which markedly exacerbates renal and gastrointestinal functions.[11] The calcium phosphate metabolism disorder that accompanies THPT has also been suggested to contribute to the pathophysiology of peptic ulcer disease, possibly affecting the gastric mucosa and leading to increased chances of gastrointestinal hemorrhage.[12] In addition, THPT causes other metabolic bone disease manifestations like osteodystrophy and fractures which compromise the quality of life for patients while on hemodialysis.[13] The issue of how to manage THPT in patients receiving hemodialysis is still unresolved.

Medical therapies employing the use of vitamin D analogs (calcitriol, paricalcitol) and calcimimetics have been noted to lower PTH levels, although they do not mitigate parathyroid hyperplasia.[14] As a result, severe or refractory THPT is remain surgically treatable (parathyroidectomy).[15] Unfortunately, surgical referral is often too late, leaving hyper parathyroid patients uncontrolled and hyperthyroid and its consequences for a longer period of time.[16] In patients with CKD and dialysis, THPT is known to be greatly underdiagnosed and undertreated, remaining cases with grave complications due to differences in diagnostic criteria, goals of treatment, and absence of guidelines.[17] Difficulties in early diagnosis of THPT arises from overlap of clinical features with SHPT, variability in definition of the PTH threshold, as well as a lack of follow-up in chronic dialysis patients. Therefore, this study aims to evaluate the incidence of THPT among CKD patients undergoing long-term hemodialysis and to identify the key risk factors contributing to its development.

METHODS

This cross-sectional study was carried out at Swat, Pakistan, In Jan and Feb 2025 with an aim on patients suffering from chronic kidney disease (CKD) on long-term hemodialysis to determine the frequency and risk factors of tertiary hyperparathyroidism (THPT). It integrated adult patients (≥18 years) on hemodialysis for no less than five years, qualifying by having elevated parathyroid hormone (PTH) levels > 300 pg/mL even after treatment for SHPT, serum calcium level > 10.5 mg/dL, and phosphate changes suggestive of THPT. Those patients having a prior history of parathyroidectomy or active malignancies perturbing calcium metabolism were excluded to prevent confounding variables that could independently alter PTH and calcium levels.

Using a power analysis, we established the sample size for this study ($\alpha = 0.05$, power = 80%), screening 200 hemodialysis patients through consecutive sampling. A total sample size of 200 was selected to achieve adequate statistical power for identifying significant predictors of THPT while ensuring representativeness of the

hemodialysis population in Swat. Clinical and biochemical data was assessed from the hospital records and laboratory reports which included demographic data (age, sex, duration of dialysis) and other available biological data, such as (calcium, phosphate, and PTH concentrations), as well as risk factors (duration of dialysis, vit D analogues, calcimimetic, or phosphate binder use), and complications (vascular calcifications, osteodystrophy, and cardiovascular diseases).

Ethical approval for this study was granted by the Ethical Committee of Miangul Abdul Haq Jahanzeb Kidney Teaching Hospital Manglor Swat (IRB No. 122). Informed consent was obtained from all participants prior to their inclusion in the study. Permissible variables were analyzed using frequencies and percentages while means ± SD was utilized for non-permissible variables. The Chi-square test was used for categorical variables, for the continuous variables, we used t-test and ANOVA followed by binary logistic regression to identify independent predictors of THPT (dependent variable: THPT Yes/No), while controlling for age, dialysis length, PTH, serum calcium, and phosphate level. Significance was set at p-value of 0.05.

RESULTS

The study comprised 200 chronic kidney disease patients undergoing hemodialysis treatment Swat, Pakistan. They were screened and assigned into THPT (n=72) and non-THPT (n=128) groups based on biochemical markers. The participants' mean age was 55.2 ± 10.8 years and male to female ratio was 60:40. The average duration of hemodialysis was 9.5 ± 4.2 years. The most prevalent comorbidities were diabetes mellitus (40%) and hypertension (65%).

Prevalence of Tertiary Hyperparathyroidism (THPT)

Out of 200 hemodialysis patients, 72 (36%) were diagnosed with THPT, based on persistently elevated parathyroid hormone (PTH) levels (>300 pg/mL), hypercalcemia (>10.5 mg/dL), and phosphate imbalance. The remaining 128 patients had either SHPT with controlled PTH levels or no significant hyperparathyroidism.

Biochemical Markers in THPT vs. Non-THPT Groups

In Table-II Patients with THPT had significantly higher levels of PTH, calcium, and phosphate, along with a greater prevalence of vitamin D deficiency. Independent t-test is used to analyze the results.

Variable	THPT (n=72)	Non-THPT (n=128)	P-Value
Total Participants	72	128	-
Mean Age (years)	56.1 ± 9.8	54.5 ± 10.3	0.21
Male (%)	43 (60%)	74 (58%)	0.65
Female (%)	29 (40%)	54 (42%)	0.78
Mean Dialysis Duration (years)	11.2 ± 3.9	8.1 ± 3.5	<0.05
Diabetes Mellitus (%)	32 (44%)	48 (38%)	0.52
Hypertension (%)	50 (69%)	80 (63%)	0.48

Table-I. Presents the baseline characteristics of study participants.

Biochemical Parameter	THPT (n=72)	Non-THPT (n=128)	P-Value
PTH (pg/mL)	412 ± 75	256 ± 48	<0.001
Serum Calcium (mg/dL)	11.1 ± 0.6	9.8 ± 0.4	<0.001
Serum Phosphate (mg/dL)	5.4 ± 1.2	4.2 ± 0.9	<0.05
Vitamin D Deficiency (%)	78%	42%	<0.05

Table-II. Summarizes the biochemical markers of THPT and non-THPT patients.

Regression Analysis for Predictors of THPT

In Table-III A binary logistic regression analysis was performed to identify independent risk factors for THPT. The model controlled for age, gender, dialysis duration, PTH levels, serum calcium, phosphate levels, and vitamin D therapy.

Complications Associated with THPT

In Table-IV Patients diagnosed with THPT experienced higher rates of complications, including vascular calcifications, fractures, and gastrointestinal issues, compared to non-THPT patients. Chi-square test is used to analyze the

results of Table-IV.

Predictor	Odds Ratio (95% CI)	P-Value
Dialysis Duration (>10 years)	2.67 (1.82–3.91)	<0.001
PTH >300 pg/mL	3.21 (2.11–4.56)	<0.001
Serum Calcium >10.5 mg/dL	2.89 (1.94–4.13)	<0.001
Lack of Vitamin D Therapy	1.98 (1.32–3.01)	0.002

Table-III. Displays the logistic regression results for THPT predictors.

Complication	THPT (n=72)	Non-THPT (n=128)	P-Value
Vascular Calcifications (%)	48%	22%	<0.05
Fractures (%)	12%	3%	<0.05
Gastrointestinal Issues (%)	18%	7%	<0.05

Table-IV. Summarizes the complication rates.

The analysis determined the rate of tertiary hyperparathyroidism (THPT) among chronic kidney disease (CKD) patients receiving hemodialysis in Swat to be 36%. Some primary contributing factors were longer dialysis periods, constant elevated levels of parathyroid hormone (PTH), hypercalcemia, and low vitamin D levels. The patients suffering from THPT presented with greater vascular complications such as calcifications and additional fractures alongside gastrointestinal problems compared to the patients not suffering from THPT.

Additionally, regression analysis using a binary logistic model validated that greater than 10 years of dialysis, hyperparathyroidism, and elevated PTH along with hypercalcemia were found to be essential determinants of THPT. The results call for stronger action in the form of early screening and adequate vitamin D supplementation along with appropriate medical care to control THPT and avert complications among patients on hemodialysis.

DISCUSSION

This study's results underscore the high burden of tertiary hyperparathyroidism (THPT) seen in chronic kidney disease (CKD) patients on long-term hemodialysis in Swat, Pakistan. The prevalence of 36% is in line with estimates from other parts of the world, raising further red flags about mineral and bone complications among CKD patients.[1] Important risk factors include long dialysis vintage (>10 years), high parathyroid hormone (PTH) levels (>300 pg/mL), hypercalcemia (>10.5 mg/dL), and absence of vitamin D treatment, which is consistent with previously published work.[2,3]

Patients with THPT had higher prevalence of vascular calcifications (48% vs 22%), fractures (12% vs 3%) and gastrointestinal problems (18% vs 7%), which illustrates the significant morbidity burden associated with this condition.[4] Vascular calcifications due to chronic hypercalcemia with phosphate dysmetabolism aggravate the already existing cardiovascular disease, which is the leading cause of death in patients on dialysis.[5] Furthermore, the increasing prevalence of fractures points to the impact of chronic parathyroid hormone dysregulation on bone metabolism, which may lead to osteodystrophy.[6,7]

In spite of having access to vitamin D substitutes and calcimimetics, many patients in this study showed inadequate PTH control, indicating possible noncompliance or treatment resistance, a concern noted before in nephrology literature.[8] Because of the resistant nature of THPT, surgical therapy by way of parathyroidectomy is the most effective treatment. However, Turkey still struggles to deliver prompt surgical intervention.[9,10] The postponement of surgical treatment aggravates disease progression even further and highlights the critically important need for established diagnostic frameworks and better treatment strategies.[11]

There is new evidence that suggests a possible genetic component to THPT, especially in the South Asian region, which is known for its vitamin D deficiency.[12,13] Furthermore, dietary intake of phosphate and the effectiveness of phosphate binders greatly impact the aetiology of secondary to tertiary hyperparathyroidism.[14,15] All these factors support the rationale for greater individualization in the treatment of THPT. A number of authors contend that non-adherence to control of phosphate allowance leads to

dysregulation of PTH gland activity, therefore emphasizing the need for stringent dietary and medicative control in chronic dialysis patients.[16,17]

Another important issue is the economic strain posed by THPT management because late-stage parathyroidectomy and hospitalization costs are well known to economically burden the healthcare systems of developing countries such as Pakistan.[18,19] The lack of medical infrastructure and inconsistent availability of calcimimetic therapy complicate effective disease control which further bolsters the need for policy-level changes to improve THPT management.[20,21] Auxiliary information from THPT neighboring countries indicates that the systematic implementation of early screening programs can drastically decrease the prevalence of THPT and its complications which further highlights the need for clinical guidelines at the national level. Moreover, emerging non-surgical therapies, especially those employing a combination of vitamin D with phosphate binders, may reduce the need for surgical interventions, but their impact over an extensive period of time has yet to be established.

CONCLUSION

This study underscores the high prevalence and complications of THPT among hemodialysis patients in Swat, Pakistan, emphasizing the urgent need for improved screening, effective medical intervention, and timely surgical referrals Key risk factors, including prolonged dialysis, persistent hyperparathyroidism, hypercalcemia, and vitamin D deficiency, must be actively monitored to prevent disease progression. Given the suboptimal response to pharmacological treatment, a multidisciplinary approach involving nephrologists, endocrinologists, and surgeons is crucial for optimizing patient outcomes. These findings highlight the necessity of integrating routine THPT screening into nephrology care, along with patient education programs to enhance adherence to phosphate binders and vitamin D therapy. Future research should focus on early intervention strategies, long-term treatment efficacy, and cost-effective management approaches to mitigate THPT-related complications in CKD patients.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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REFERENCES

1. Zhang LX, Zhang B, Liu XY, Wang ZM, Qi P, Zhang TY, et al. **Advances in the treatment of secondary and tertiary hyperparathyroidism.** Front Endocrinol (Lausanne). 2022 Dec 6:13:1059828. doi: https://doi.org/10.3389/fendo.2022.1059828

2. Cozzolino M, Ureña-Torres P, Vervloet MG, Brandenburg V, Bover J, Goldsmith D, et al. **Is chronic kidney disease-mineral bone disorder (CKD-MBD) really a syndrome?** Nephrol Dial Transplant. 2014; 29(10):1815-20. DOI https://academic.oup.com/ndt/article/29/10/1815/2325960

3. Dream S, Kuo LE, Kuo JH, Sprague SM, Nwariaku FE, Wolf M, et al. **The American Association of Endocrine Surgeons Guidelines for the definitive surgical management of secondary and tertiary renal hyperparathyroidism.** Ann Surg. 2022 Sep 1; 276(3):e141-e176. DOI: https://journals.lww.com/annalsofsurgery/abstract/2022/09000/the_american_association_of_endocrine_surgeons.18.aspx

4. La Rosa S. **Hyperaldosteronism.** Endocr Pathol. 2022 Nov 25; pp. 378-80. doi: https://link.springer.com/referenceworkentry/10.1007/978-3-030-62345-6_5250

5. Leung EKY. **Parathyroid hormone.** Adv Clin Chem. 2021; 101:41-93. doi: https://doi.org/10.1016/bs.acc.2020.06.005.

6. Drüeke TB. **Hyperparathyroidism in chronic kidney disease.** NCBI Bookshelf. 2021 Oct 18. Available from: https://www.ncbi.nlm.nih.gov/books/NBK278975/.

7. Khamis SSA, El Edel RH, Zahran AM, Ibrahim MA, El Zorkany KMA. **Prevalence of chronic kidney disease in relatives of chronic hemodialysis patients.** Open J Nephrol. 2020 Dec; 10(4):270-82. doi: 10.4236/ojneph.2020.104027.

8. Nitta K. **Nontraditional risk factors for cardiovascular disease in patients on peritoneal dialysis.** Ren Replace Ther. 2024 Apr 12; 10:25. doi: 10.1186/s41100-024-00536-0. Available from: https://rrtjournal.biomedcentral.com/articles/10.1186/s41100-024-00536-0

9. Sutton W, Chen X, Patel P, Karzai S, Prescott JD, Segev DL, et al. **Prevalence and risk factors for tertiary hyperparathyroidism in kidney transplant recipients.** Surgery. 2021 Jul 12; 171(1):69-76. doi: 10.1016/j.surg.2021.03.067. https://pmc.ncbi.nlm.nih.gov/articles/PMC8688275/

10. Ghonimi T, Hamad A, Fouda T, AlAli F, Ezzat M, Awad M, et al. **Cardiovascular calcification in hemodialysis patients: A Qatar-based prevalence and risk factors study.** Qatar Med J. 2024 Mar 14; 2024(1):18. 10.5339/qmj.2024.18. https://pmc.ncbi.nlm.nih.gov/articles/PMC11037094/.

11. Sadiq NM, Anastasopoulou C, Patel G, Badireddy M. Hypercalcemia. **In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2024 May 7.** Available from: https://www.ncbi.nlm.nih.gov/books/NBK430714/.

12. Malik TF, Gnanapandithan K, Singh K. **Peptic ulcer disease.** In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2023 Jun 5. Available from: https://www.ncbi.nlm.nih.gov/books/NBK534792/.

13. Hu L, Napoletano A, Provenzano M, Garofalo C, Bini C, Comai G, et al. **Mineral bone disorders in kidney disease patients: The ever-current topic.** Int J Mol Sci. 2022; 23(20):12223. doi: 10.3390/ijms232012223. Available from: https://doi.org/10.3390/ijms232012223

14. Liu X, Liu Y, Zheng P, Xie X, Li Z, Yang R, et al. **Effects of active vitamin D analogs and calcimimetic agents on PTH and bone mineral biomarkers in hemodialysis patients with SHPT: A network meta-analysis.** Eur J Clin Pharmacol. 2024 Oct; 80(10):1555-1569. doi: 10.1007/s00228-024-03730-5.

15. Masaki C, Ogawa S, Shima H, Banno T, Tsuyuguchi M, Nagasaka N, et al. **Parathyroidectomy for tertiary hyperparathyroidism after second kidney transplantation: A case report.** EN Case Rep. 2020 Oct 20; 10(2):208-13. doi: 10.1007/s13730-020-00545-y.

16. Uludag M, Unlu MT, Kostek M, Caliskan O, Aygun N, Isgor A. **Persistent and recurrent primary hyperparathyroidism: Etiological factors and pre-operative evaluation.** Sisli Etfal Hastan Tip Bul. 2023 Mar 21; 57(1):1-17. doi: 10.14744/SEMB.2023.39260.

17. Muppidi V, Meegada SR, Rehman A. **Secondary hyperparathyroidism.** In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Aug 28. Available from: https://www.ncbi.nlm.nih.gov/books/NBK557822/.

18. Rugnath K, Kinoo SM. **Feasibility of focused parathyroidectomy in developing countries—a scoping review.** Gland Surg. 2024 Jun 20; 13(6):1054-65. doi:10.21037/gs-24-57. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC11247565/.

19. Deering KL, Larsen NJ, Loustau P, Weiss B, Allas S, Culler MD, et al. **Economic burden of patients with post-surgical chronic and transient hypoparathyroidism in the United States examined using insurance claims data.** Orphanet J Rare Dis. 2024 Apr 18; 19:164. doi:10.1186/s13023-024-03155-4. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC11025287/.

20. Mathur A, Sutton W, Ahn JB, Prescott JD, Zeiger MA, Segev DL, et al. **Association between treatment of secondary hyperparathyroidism and posttransplant outcomes.** Transplantation. 2021 Dec 1; 105(12):e366–e374. doi:10.1097/TP.0000000000003653. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC8313633/.

21. Zhang Q, Li M, You L, Li H, Ni L, Gu Y, et al. **Effects and safety of calcimimetics in end-stage renal disease patients with secondary hyperparathyroidism: A meta-analysis.** PLoS One. 2012 Oct 25; 7(10): e48070. doi: 10.1371/journal.pone.0048070. Available from: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0048070.

AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Akbar Khan:** Conceptualization.
2	**Muhammad Najumusaqib:** Methodology.
3	**Zainab:** Methodology, conceptualization.
4	**Shabir Ali:** Analysis.
5	**Hazir Ullah:** Writing review, editing.
6	**Aziz Ur Rahman:** Writing review, editing.