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**Original Research Article**

# A study of secondary hyperparathyroidism in patients with chronic kidney disease in a tertiary care hospital

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## ABSTRACT

**Background:** Secondary hyperparathyroidism (SHPT) is one of the less recognized complications in patients with chronic kidney disease (CKD). The prevalence of SHPT in various stages of CKD was evaluated by measuring the levels of intact parathyroid hormone (iPTH).
**Methods:** This cross-sectional study was carried out in 100 CKD patients. Serum creatinine, calcium, phosphorous and iPTH levels were measured and statistical analysis was carried out using the SPSS software (IBM, NY, USA).
**Results:** Among the 100 participants, the mean age (SD) was 59.3 (7.8) years. In our study population, 52% were men and the rest were females. Hypertension (75%) was the most common chronic morbidity. Prevalence of hyperparathyroidism among chronic kidney disease patients was 22% (95% CI: 14.7-30.9%). The prevalence of secondary hyperparathyroidism among dialysis and non-dialysis patients were 30% and 14% respectively which was statistically significant.
**Conclusions:** SHPT is an important complication which is often underdiagnosed. Secondary hyperparathyroidism starts to develop when eGFR falls below 60ml/min. PTH levels starts to rise as the disease progress. Hence it is important for the treating physicians to monitor the PTH levels early in the course of CKD to prevent and treat bone mineral disease.

**Keywords:** Chronic kidney disease, CKD, Intact parathyroid hormone, iPTH, Secondary hyperparathyroidism, SHPT

## INTRODUCTION

Chronic Kidney Disease (CKD)is a common clinical disorder which is constantly increasing among the population.[1] In spite of various etiologies, CKD is the final common pathway of irreversible destruction of nephrons, ultimately resulting in "alteration of milieu interior" affecting every system in the body. Patients with moderate disease is found with abnormalities in bone metabolism and considerable mortality.[2] Although there are various causes of chronic kidney disease, diabetes and hypertension contribute significantly. The early detection of the disease helps in proper management leading to decrease in renal and cardiovascular mortality due to the disease.

Secondary hyperparathyroidism is a complication of CKD which often results in bony abnormalities, calcifications in blood vessels and cardiovascular consequences.[3] CKD leads to deranged calcium and phosphorous metabolism of the body and leading to various abnormalties in the body.[4] Our study was done to measure serum intact parathyroid hormone (iPTH) levels and to find out the prevalence of secondary

hyperparathyroidism among various stages of chronic kidney disease patients and also comparing intact parathyroid hormone (iPTH) among dialysis and non-dialysis patients.[2,3]

## METHODS

This study was conducted after approval from institutional review board and fully informed consent from patients. This was a facility based cross sectional study conducted among patients attending Saveetha Medical College and Hospital, Chennai, India.

Our study was conducted for a period of 1 year. A total of 100 patients aged more than 20 years, either attending OPD or admitted were included in the study after they were screened using the exclusion and inclusion criteria.

### *Inclusion criteria*

Patients with CKD aged >20 years, in varying stages of severity.

### *Exclusion criteria*

- Patients with Acute Kidney Injury (AKI)
- Patients with primary hyperparathyroidism.

### *Criteria for chronic kidney disease*

Presence of objective kidney damage for atleast three months. Kidney damage defined as pathologic abnormalities or markers of damage including abnormalities in blood or urine tests or imaging studies.

Glomerular filtration rate (GFR) less than 60ml/min/1.73m$^2$ for at least three months with or without kidney damage.

### *Glomerular filtration rate*

The estimated glomerular filtration rate was calculated using CKD-EPI equation:

GFR = 141 × min (SCr/κ, 1)α × max(SCr/κ, 1)-1.209 ×0.993Age

Multiply by 1.018 for women,

Where, SCr is serum creatinine in mg/dL, κ is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the minimum of SCr/κ or 1, and max indicates the maximum of SCr/κ or 1.

### *Classification of CKD*

The NKF classification as follows[5]

- Stage I with GFR > or = 90ml/min/1.73m$^2$,
- Stage II with GFR between 60-89 ml/min/1.73m$^2$,
- Stage III with GFR between 30-59 ml/min/1.73m$^2$,
  -Stage III a-30-44 ml/min/1.73m$^2$
  -Stage III b-45-59 ml/min/1.73m$^2$
- Stage IV with GFR between 15-29 ml/min/1.73m$^2$, and
- Stage V with GFR <15ml/min/1.73m$^2$.

Detailed clinical history was taken from all the patients who were included in the study. Past history of hypertension, diabetes mellitus, and any drug intake was taken. All the patients were examined clinically in detail. The following investigations were done by collecting blood samples and ultra-sonogram of abdomen was done.

- Blood urea
- Serum creatinine,
- Estimated glomerular filtration rate,
- Serum calcium
- Serum phosphorus,
- Intact parathyroid hormone (iPTH) level.

### *Criteria for secondary hyperparathyroidism*

The criteria for diagnosis of secondary hyperparathyroidism are a low-normal serum calcium, high serum phosphorous and elevated serum parathyroid hormone levels. Normal values:

- Serum calcium-8-11mg/dl
- Serum phosphorus-2.5-4.5mg/dl
- Serum iPTH-15-65mg/dl

### *Statistical analysis*

Data was entered using Microsoft excel and analysis was done using SPSS version 20. Continuous variables like age were summarized as mean and standard deviation. Categorical variables were summarized as proportions. Prevalence of secondary hyperparathyroidism was reported with 95% confidence interval. Chi square test was used to assess the association between secondary hyperparathyroidism and various stages of CKD. 'p' value less than 0.05 were considered statistically significant.

## RESULTS

The age of the study participants ranged from 28 to 87 years with Mean (SD) of 59.3 (7.8) years (Table 1). In our study 52% were men and the rest were females. (Figure 1). Hypertension (75%) was the most common chronic morbidity among the participants followed by diabetes mellitus (55%). Among the study participants 50% had end stage renal disease (Figure 2).

Majority of the patients (71%) had blood urea levels ranging from 41 to 80mg/dl. The mean serum creatinine level measurement was 3.29mg/dl. About three fourth (75%) of study population had serum creatinine levels

ranging from 1.3 to 5mg/dl. The mean serum calcium level measurement was 8.45mg/dl. Majority of the patients, (61%) had serum calcium levels ranging from 8.1 to 11mg/dl. The mean serum phosphorus level measurement was 4.6 mg/dl. More than half (52%) of study population had serum phosphorus levels >4.5mg/dl (Table 2).

**Table 1: Socio-demographic details of the study participants (N=100).**

| Characteristics | Frequency, N (%) |
|---|---|
| **Age category (in years)** | |
| 20-40 | 8 (8%) |
| 41-60 | 47 (47%) |
| >60 | 45 (45%) |
| **Gender** | |
| Male | 52 (52%) |
| Female | 48 (48%) |
| **Chronic co-morbidity** | |
| Hypertension | 75 (75%) |
| Diabetes Mellitus | 55 (55%) |
| **Stages of CKD** | |
| Stage I | 5 (5%) |
| Stage II | 12 (12%) |
| Stage III | 16 (16%) |
| Stage IV | 17 (17%) |
| Stage V | 50 (50%) |

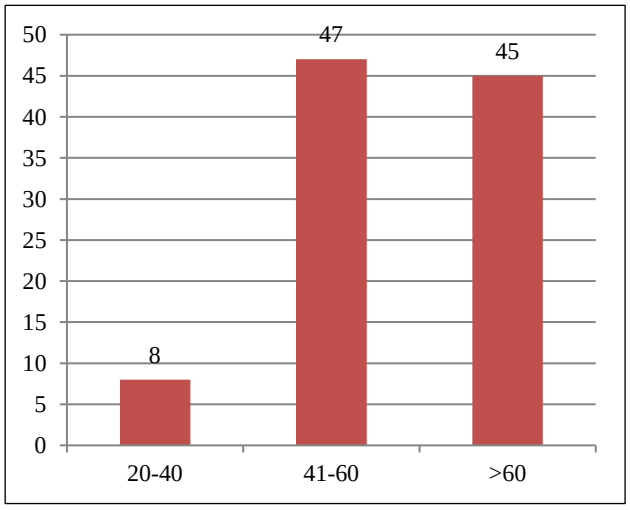


**Figure 1: Age distribution of the study participants (n=100).**

Distribution of various stages of chronic kidney disease showed stage V (ESRD)-50% with maximum no. of patients. The distribution of population among the stages of CKD are shown in (Figure 3). The mean estimated glomerular filtration rate was 27.1ml/min. Prevalence of hyperparathyroidism among chronic kidney disease patients was found to be 22% (95% CI: 14.7-30.9%). Table 3 shows the association between secondary hyperparathyroidism and the stages of CKD. There was a statistically significant difference between the prevalence of secondary hyperparathyroidism among non-dialysis patients (14%) and dialysis patients (30%) (Figure 4, 5).

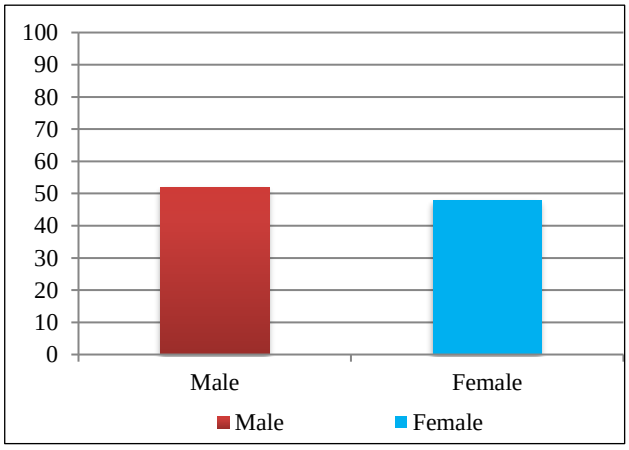


**Figure 2: Gender distribution of the study participants (n=100).**

**Table 2: Biochemical parameters of the study participants (N=100).**

| Serum calcium | Frequency |
|---|---|
| ≤ 8 mg/dl | 35 (35%) |
| 8.1-11 mg/dl | 61 (61%) |
| >11 mg/dl | 4 (4%) |
| **Serum phosphorus** | |
| < 2.5 mg/dl | 10 (10%) |
| 2.5-4.5 mg/dl | 38 (38%) |
| > 4.5 mg/dl | 52 (52%) |
| **Serum parathyroid hormone** | |
| ≤ 65 pg/ml | 52 (52%) |
| >65 pg/ml | 48 (48%) |

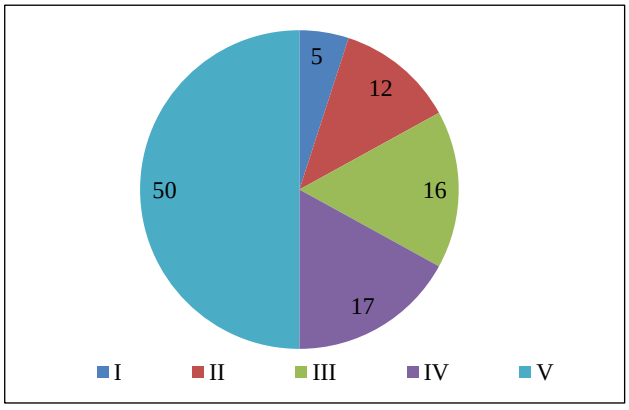


**Figure 3: Distribution of study participants based on the stages of CKD (n=100).**

## DISCUSSION

In our study the mean age group was 59.3 (7.8) years which was similar to study by Das et al.[6] Prevalence of

hyperparathyroidism among chronic kidney disease patients was found to be 22% (95% CI: 14.7-30.9%). In relation to the co morbidities, diabetics were 55% which was similar to study Lea JP et al.[7] In case of hypertension, our study was in contrast to previous studies which showed 70% hypertensive explained by Abraham G et al.[8] Similar study conducted in Chennai also showed similar prevalence of around 26% among CKD patients.[9]

**Table 3: Association between stages of CKD and secondary hyperparathyroidism (N=100).**

| Stage of CKD | Total, N | Secondary hyperparathyroidism, n (%), (n=22) | $X^2$ | P-value |
|---|---|---|---|---|
| Non-dialysis CKD (stage I-IV) | 50 | 7 (14%) | 3.72 | 0.05 |
| Dialysis CKD (stage V) | 50 | 15 (30%) | | |

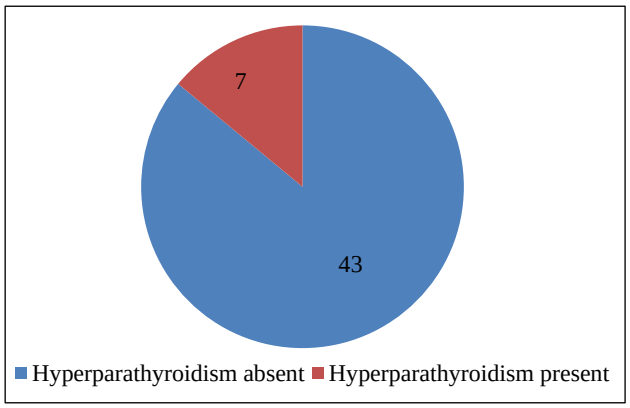


**Figure 4: Secondary hyperparathyroidism in CKD stages I-IV.**

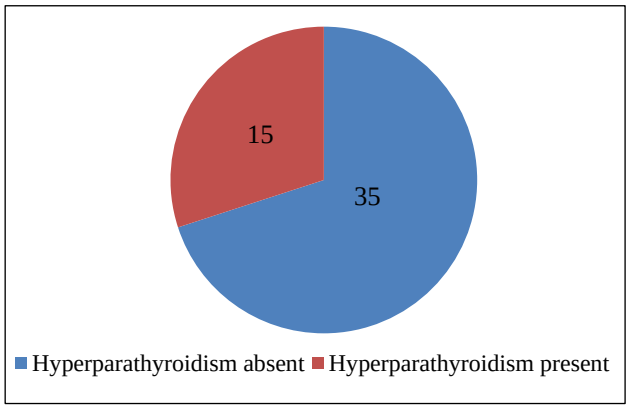


**Figure 5: Secondary hyperparathyroidism in CKD stage V.**

Current study showed that the patients requiring dialysis (stage V CKD) had significantly higher chance of having secondary hyperparathyroidism when compared to non-dialysis patients (stage I-IV CKD).[10] These were similar to findings in the study conducted by Levin A et al, where patients belonging to stage IV and V had higher prevalence of secondary hyperparathyroidism when compared to the Stage I-III.[11,12] CKD stage V patients who are on dialysis are most likely to have secondary hyperparathyroidism which was similar to our study.[13]

Current study also adds to the limited literature available regarding the association between the secondary hyperparathyroidism and stages of CKD. FGF-23, an important biomarker which can be helpful in identifying secondary hyperparathyroidism as early as stage 3. However, the study has certain limitations. Since this was a cross sectional study, causal effect cannot be inferred between stage of CKD and secondary hyperparathyroidism. This was shown by Ketteler et al, where SHPT can occur in early stages of chronic kidney disease.[14] Further longitudinal studies with larger sample size may be required to study the true association between CKD and serum PTH levels.

Current treatment options for the condition includes the phosphate binders, dietary restriction of phosphates, vitamin D, total PTH, calcitriol or vitamin D analogues. These have been found to be only partially successful in managing the secondary hyperparathyroidism and not always effective sufficiently in lowering the parathyroid hormone, calcium and phosphorus to the desired levels. A calcimimetic agent like cinacalcet directly controls the secretions of PTH by acting at the level of parathyroid gland.[15] It can also simultaneously reduce the calcium and phosphorus level representing major advances in the therapy.[7]

## CONCLUSION

Our study found that more than one-fifth of the CKD patients had secondary hyperparathyroidism. It was found that significant association between stages of CKD and secondary hyperparathyroidism especially in patients belonging to Stage V. They had significantly higher prevalence when compared to patients in other stages. Secondary hyperparathyroidism is associated with mortality and morbidity in CKD. It can occur in earlier stages and through measurement of serum iPTH, it can be diagnosed earlier, and appropriate treatment can be instituted.

Reinforcement of medication adherence, diet and physical activity and provision of positive reinforcement

across the disciplines is very crucial in successfully managing the secondary hyperparathyroidism.

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