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### PREVALENCE OF SECONDARY HYPERPARATHYROIDISM IN CHRONIC KIDNEY PATIENTS

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CKD-Chronic Kidney Disease

#### ABSTRACT

Secondary hyperparathyroidism occurs mainly due to chronic kidney disease which aggravates from stage 1-5, which is due to imbalance between calcium and phosphorous homeostasis. Secondary hyperparathyroidism is the serious issue to be considered because of its complications including cardiovascular disease soft tissue and vascular calcification calcific uremic arteriopathy (CUA). Our study was to find the prevalence of secondary hyperparathyroidism that would help to find out the epidemiological spread of the disease that would help in improving the treatment effectiveness for the safety of the subjects. our study includes 60 subjects who are undergoing dialysis from 12 to 48 months of duration we found high prevalence of secondary hyperparathyroidism with 66.6 % patients with IPTH levels over 300pg/ml, 83% of the patients were found to be hypocalcaemia and 75% of the patients were found to be having abnormal phosphorous levels with majority having high phosphorous levels so based on our study prevalence of secondary hyperparathyroidism was high which would results in serious complications like bone dystrophy which left untreated would result to death. The final result of our study include majority of the patient have secondary hyperparathyroidism which would results in further complications like bone dystrophy and cardiovascular abnormality left untreated would result in further menacing complications which left untreated would may lead to death of the patients.

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## INTRODUCTION

Secondary hyperparathyroidism starts as an adaptive process but as the disease progresses it develops as a maladaptive process leading to mineral bone disease [1]. As kidney function decreases, there is gradual deterioration in mineral homeostasis resulting in disruption of serum and tissue concentrations of phosphorus and calcium, as well as alteration in circulating levels of hormones such as parathyroid hormone (PTH), 25-hydroxyvitamin D [25(OH)D], 1,25-dihydroxyvitamin D [1, 25(OH)2D], fibroblast growth factor-23 (FGF-23), and growth hormone<sup>[2]</sup>. Due to impairment of the kidney there is imbalance between calcium and phosphorus homeostasis which leads to accumulation of phosphorus in the body and decreased reabsorption of calcium which stimulates parathyroid gland to produce more parathyroid hormone. As kidney function decreases there is decreased synthesis of Calcitriol and elevated levels of Phosphatonin levels which indirectly affects calcium and phosphorus homeostasis thus increasing parathyroid hormone levels [1,3]. That would result in secondary hyperparathyroidism. The gradual elevation of secondary hyperparathyroidism occurs in chronic kidney disease with 40% in Stage 3 and goes as high as 80% in stage 5 [4]. Our study is based on the research carried out by Joy et al in 2007 who calculated that within 2 to 4.7 million people with CKD suffer with elevated parathyroid levels [5]. According to the study done by Salem in 1997 prevalence of secondary hyperparathyroidism is not related to geographical location, race, and ethnicity [6]. Patients with CKD are prone to high risk of bone disorders, vascular abnormalities, and mortality due to calcium and phosphorus homeostasis which occurs in secondary hyperparathyroidism [7]. Secondary hyperparathyroidism does not develop in the late stage of CKD; instead, it develops in the early stage and progresses as kidney functions decline [8]. ALP levels need to be assessed because due to increased bone disorders there is increased osteoclast activity which causes bone to degrade; to prevent this action there is increased osteoblast activity to compensate bone loss which produces high alkaline phosphatase levels.

## METHODOLOGY

This cross-sectional study was carried out on end-stage renal disease patients in Narayana Hrudhaya multispecialty hospital, nephrology department, Suraram X Roads, Jeedimetla, Hyderabad 500015, which is a 500-bedded hospital during the year 2016-2018. This study got approval from the institutional ethical committee before initiating. Total 60 patients who are undergoing hemodialysis with various causes were recorded with their age, sex, and weight on the treatment plan. Every patient receives vitamin D analogues and calcium supplements like cinacalcet for co-morbid conditions. Every patient has either diabetes mellitus or hyperparathyroidism.

## EXCLUSIVE CRITERIA

Patients with acute renal failure and those subjects in which the primary cause is other than chronic kidney disease (Vitamin D Deficiency, Intestinal Bypass Surgery) were excluded from the study. Patients with primary hyperparathyroidism which occurs due to parathyroid cancer or parathyroid surgery were excluded in the study.

## LABORATORY METHODS

PTH was assayed through Bayers Automated Chemiluminisence system. Serum Calcium was estimated by Arsenazo method. Serum inorganic phosphate was analysed using Ammonium Molybdate method. The above-mentioned details were obtained from clinical assessment records including medical records and other relevant sources.

## RESULTS

This study includes a total of 61 patients in which 11(18%) were females and 49(82%) were males, their duration of hemodialysis range from 8 to 300 months with average of 73 months. The subjects enrolled in the study were between 20-80 years of age. Subjects with age group between 20-40 years were found to be 30%, subjects with the age 40-60 years were found to be 50%, and subjects with the age group between 60-80 years were found to be 20% with mean age  $48 \pm 13.69$ . 37 patients were found to have hypertension and 23 patients were found to have diabetes mellitus, all patients were found to have abnormal levels of haemoglobin.

Table 1: PTH distribution in the study.

PTH Range (pg/ml)	Number of Subjects
<150	08
150-300	12
300-400	19
400-500	9
500-600	6
600-700	4
700-800	1
800-900	1

Normal Range 10-65pg/dl, with accepted levels between 150-300pg/ml

Among 60 patients in the study 8 patients have PTH levels less than 150pg/ml, 12 patients have PTH value between 150-300pg/ml, and 40 patients have PTH levels above 300pg/ml with mean  $348\pm16$ .

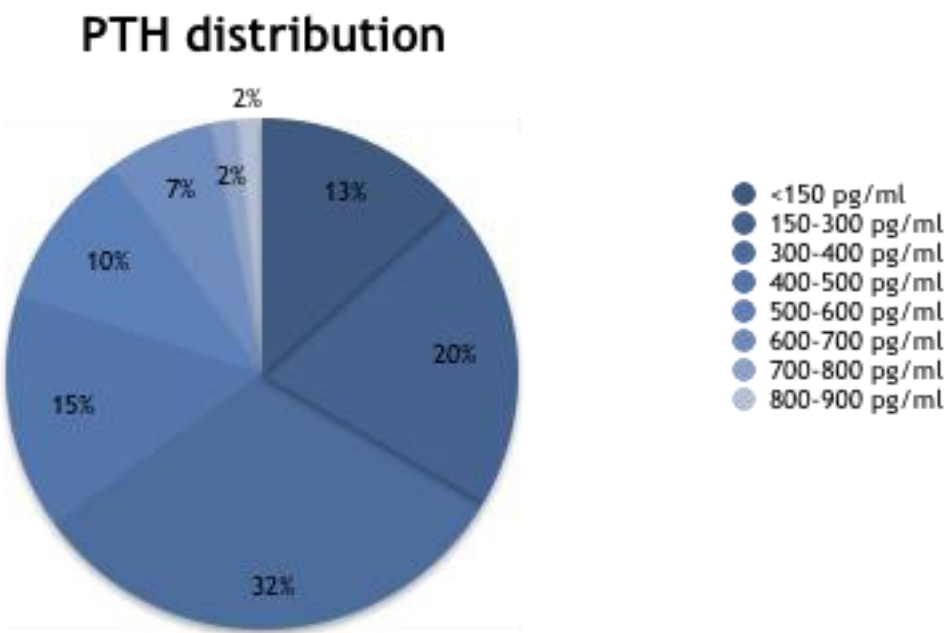


Figure 1: percentage of people with various levels of intact parathyroid hormones in blood.

Table 2: Calcium distribution in the study.

Calcium levels(mg/dl)	Number of Subjects
<8.5	50
8.5-10.2	10
>10.2	0

Normal range 8.5 to 10.2 mg/dl.

Among 60 patients in the study 50 patients were found to have hypocalcaemia and 10 patients were found to be within the normal range with mean  $7.6\pm1.10$ .

## Calcium distribution



Figure 2: percentage of people with various levels of Calcium in the blood.

Table 3: Phosphorous distribution in the study.

Phosphorus levels(mg/dl)	Number of Subjects
<2.5	7
2.5-4.5	15
4.5-9	38

Normal Range 2.5-4.5 mg/dl

Most of the patients were having abnormal levels of Phosphorous, 7 patients were having Phosphorous levels below 2.5 mg/dl, 38 patients were having more than 4.5mg/dl, and 15 patients were having normal range of 2.5-4.5mg/dl with mean  $4.88 \pm 1.5$ .

## Phosphorous distribution

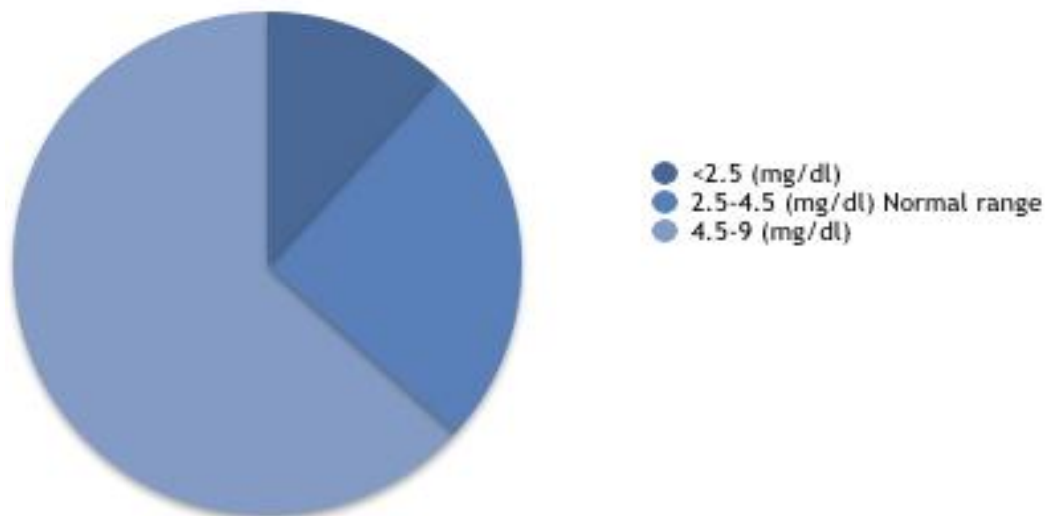


Figure 3: percentage of people with various levels of phosphorous in blood.

**Table 4: Alkaline phosphate distribution in the study.**

Alkaline Phosphate(u/l)	Number of Subjects
<100	11
100-200	40
200-300	5
300-400	2
400-500	1
500-600	1

Normal Range 44-107u/l

In this study most of the patients (48) were found to be having high levels of alkaline phosphate and 12 patients have normal levels with mean  $155.5 \pm 89.1$

**Table 5: Serum creatinine distribution in the study.**

Serum creatinine (mg/dl)	Number of Subjects
<4	4
4-8	19
8-12	24
12-16	9
16-20	3

Normal range 0.6-1.2 mg/dl

Every patient in our study seems to have abnormal levels of creatinine with mean  $9.1 \pm 3.88$  mg/dl

**Table 6: Laboratory parameters with normal range and their deviation from the mean.**

Lab Parameter	Mean $\pm$ Standard deviation	Normal Range
Hemoglobin	$8.62 \pm 1.80$	13-17.5g/dl
Calcium	$7.58 \pm 1.10$	12-15.5g/dl
Phosphorous	$4.67 \pm 1.56$	8.5-10.2mg/dl
Alkaline Phosphate	$155.5 \pm 89.1$	44-107iu/l
Albumin	$3.2 \pm 0.7$	3.5-5.5g/dl
Parathyroid Hormone	$348 \pm 169.66$	10-6.5pg/ml
Serum Creatinine	$9.49 \pm 3.85$	0.6-1.2mg/dl

## DISCUSSION

As secondary hyperparathyroidism is severe issue that to be taken into consideration because of its complications like cardiovascular disease increased bone turn over, our study was done to find out the prevalence of SHPT, so that new treatments and managements would be implemented to prevent those problems .Our study is based on the study done by Douthet WG in 2013 who studied about the prevalence of SHPT in chronic kidney patients on dialysis, on 1220 patients in 25 dialysis centres, in which 24% of the patients have PTH levels below 150 and 54.5% of patients have PTH levels above 300. 51.6 % patients have normal level of calcium and 51.6 patients have normal level of phosphorous [9]. Some studies have been carried out to find the prevalence of SHPT between diabetic and non diabetic patients, one was the study done by Arevalo in 2016 on prevalence of SHPT between diabetic and non diabetic patients on 409 patients. In this 60 % of diabetic patients have abnormal PTH levels and 65% of non diabetic patients have abnormal levels of PTH [10]. A similar study was done by Ali owda in 2003 on 122 patients in 2 dialysis centres in Michigan. 78% of these patients have IPHT levels above 200pg/ml and 3% of the patients have their PTH levels below 100pg/ml. They found no difference between diabetic and non diabetic patients [11]. A similar study done by Fatemeh Hayati on 112 patients in 2016, 69.6% patients has IPHT levels above the normal range and there was no difference between diabetic and non diabetic patients [14], this confirms that between diabetes and non diabetes patients prevalence of SHPT was similar. Some studies have been done without assessing the co-morbid conditions like diabetes and Hypertension, this includes the study done by Juan Carlos Bureo in 2015 at internal medicine department on 415 patients with stage 3 and 4 chronic kidney disease. In this 62.9% of the patients have PTH levels above 70pg/ml and 32.7% of the patients have PTH levels above 110pg/ml [12]

Another study done by Ayham Haddad in 2015 on 276 patients where patients receive hemodialysis therapy in three different dialysis centres found that 77.5% patients have abnormal levels of PTH with average IPHT levels 887.1pg/ml [13]. But based on the DOPPS (Dialysis Outcome And Practice Pattern Study) which was multinational and widely accepted study done on 24392 End stage renal disease patients in 5 European countries, usa and Japan about bone and mineral metabolism disorder and their management in which, only 26.7 % of the patients have IPHT levels above 300pg/ml which is very low comparing to our study [15]. Few studies have been carried out to find the conjectural effects of increased parathyroid hormone in which one of the study was done by Takanobu et al in 2002 based on their study conjectural and corneal calcification developed with abnormal mineral metabolism that results in increased bone turn over [17]. The complications of secondary hyperparathyroidism include significant bone disease, other common complications include soft tissue and vascular calcification and calcific uremic arteriolopathy (CUA) and cardiovascular disease that may results in cardiovascular morbidity and mortality in CKD patients. less common causes include neurological disturbances, haematological abnormalities and endocrine dysfunction [16]

The results of our study were similar to majority of the researchers which show 66.6 % of the patients have pth levels above the normal range and 83% of the patients have abnormal levels of calcium and 75 % of the patients have abnormal phosphorous levels. Our study include abnormal bone and mineral metabolism markers based on the normal levels suggested by k/doqi guidelines . According to k/doqi guidelines (2005) to achieve adequate control on secondary hyperparathyroidism the serum PTH levels must be between 150-300pg/ml, serum phosphorous levels should be between 3.5-5.5pg/ml and serum calcium levels should be between 8.4 to 9.5pg/ml [18]

## CONCLUSION

The final result of our study include majority of the patient have secondary hyperparathyroidism which would results in further complications like bone dystrophy and cardiovascular abnormality left untreated would result in further menacing complications which left untreated would may lead to death of the patients.

## CONFLICT OF INTEREST:

There are no conflicts of interest amongst the authors.

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