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# Oxidant and Antioxidant Imbalance in Urolithiasis Patients

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**Abstract**

***Context:*** Disturbances in mineral metabolism are commonly seen in patients with chronic renal failure. But there are very few studies on their prevalence in Indian dialysis population.

***Aim:*** To know the prevalence of secondary hyperparathyroidism in patients with stage 5 chronic kidney disease on maintenance hemodialysis.

***Settings and Design:*** Hospital based cross sectional study.

***Methods and Material:*** This study was done on 85 patients undergoing maintenance hemodialysis for ≥ six months and data was collected between January 2018 and December 2018, for a period of one year.Patients were examined for clinical features of secondary hyperparathyroidism and serum calcium, phosphorus, alkaline phosphatase, 25 hydroxy vitamin D and intact parathyroid hormone levels were measured.

***Statistical analysis used:*** The data was analysed with SPSS using Descriptive statistics, Chi-square testand significance by p value.

***Results :*** Various mineral, bone abnormalities in our study population were as follows- hypercalcemia (5.88%), hypocalcemia (36.47%), hyperphosphatemia (30.59%), hypophosphatemia (28.24%), hyperparathyroidism (36.48%), hypoparathyroidism (10.59%), deficiency of vitamin D(52.94%) and insufficiency of vitamin D (20%).

***Conclusions:*** Prevalence rate of secondary hyperparathyroidism was 36% in our study and 40% had over suppresion of iPTH levels. One third of our patients had a risk of adynamic bone disease.

***Keywords:*** Chronic kidney disease; Secondary hyperparathyroidism; hemodialysis.

## Introduction

CKD stage 5 is loss of renal function requiring renal replacement therapy,with significant complications and its prevalence has increased imposing burden for health care system.[1]

Secondary hyperparathyroidism (SHPT) represents alteration in bone, mineral metabolism caused by reduced kidney function with increased mortality.[2] It is important to diagnose SHPT, as its early treatment slows the progression of bone and cardiac complications and to know its prevalence in this dialysis population to adopt appropriate health policies. Hence this study was done to know the prevalence, biochemical and clinical profile of secondary hyperparathyroidism in chronic hemodialysis patients.

## Materials and Methods

- This was a cross sectional study, done on 85 Chronic Kidney Disease stage 5 patients of 18 years and above, on maintenance hemodialysis for ≥ 6months in KLE's Dr Prabhakar Kore Hospital and Medical Research Center, Belagavi, willing to participate in the study. Patients on glucocorticoids, bisphosphanates, nonsteroidal anti-inflammatory drugs, phenytoin or warfarin, patients with rheumatologic disease, primary parathyroid disorder, patients with history of liver disease, bone fracture in last six months prior to enrollment, were excluded from study. Institutional ethical clearance and informed consent from each individual participant was obtained.
- Stage of Chronic kidney disease was defined according to K/DOQI criteria.[3] eGFR was calculated by using Cockcroft-Gault formula. After taking informed consent, patient's details and a detailed clinical history was obtained for symptoms suggestive of secondary hyperparathyroidism.
- All patients were clinically examined including general physical examination, careful examination of the Joints, examination of cardiovascular system, respiratory system, per abdomen and nervous system for the signs of secondary hyperparathyroidism.
- After taking the informed consent, about 6ml of blood was drawn at start of hemodialysis session to measure serum calcium, phosphorus, alkaline phosphatase, calcitriol and intact Parathyroid hormone, creatinine and albumin.
- Serum intact parathyroid hormone was measured by electrochemiluminescence immunoassay, but not the fragments of it, which will also be increased in renal failure.
- Serum calcitriol was measured by chemiluminescence immunoassay, Alkaline phosphatase by King and Amstrong method, serum calcium by 5-nitro -5 methyl BAPTA method and serum phosphorus by phosphomolybdate UV Kinetic method.

***Statistics***: The information collected from the patients was noted in master chart. Analysis of data was done using statistical software version SPSS 20.00, Descriptive statistics including frequency, percentage, mean and SD, Chi-square for independence, Karl Pearson's correlationcoefficient for relationship were used and statistical significance was set at 5% level with $p<0.05$ considering significant.

***Results:*** A total of 85 patients underwent maintenance hemodialysis for an average of 24±13 months and 9.27 hours per week, Diabetes Mellitus was major cause of CKD in 49.41 % of patients

**Table 1:** Distribution of subjects based on the age groups.

| Age Group | No. of Patients | % |
|---|---|---|
| **20 to 40** | 14 | 16.47 |
| **41 to 60** | 40 | 47.05 |
| **61 to 80** | 31 | 36.47 |
| **>80** | 0 | 0 |
| **TOTAL** | 85 | 100 |

**MEAN ± SD = 54.68± 12.46**

The mean age of the study population was 54.68 ±12.46 years and ranged from 23 years to 76 years, majority being in the age group of 41- 60 years(47.05%).

**Table 2:** Distribution of subjects by gender.

| Gender | Number | Percentage |
|---|---|---|
| **Female** | 17 | 20 |
| **Male** | 68 | 80 |
| **TOTAL** | 85 | 100.00 |

Males formed majority with 80 % of the study population as compared to females (20%)

**Table 3:** Distribution of subjects based on value of serum corrected calcium.

| Corrected Calcium( in mg/di) | Number | Percentage |
|---|---|---|
| <8.4 | 31 | 36.47 |
| 8.4-9.5 | 40 | 47.06 |
| 9.6-10.2 | 9 | 10.59 |
| **>10.2** | **5** | **5.88** |
| **TOTAL** | 85 | 100 |
| **MEAN ±SD= 8.71 ± 1.09** | | |

47.06 % of patients had acceptable levels of serum corrected calcium (8.4 - 9.5 mg/dl), 36.47 % of patients had values below and 16.47% of patients above theaccepted range. 5.88% of patients had hypercalcemia (> 10.2mg/dl).

**Table 4:** Distribution of subjects based on serum phosphorus levels.

| Phosphorus ( in Mg/Dl) | Number | Percentage |
|---|---|---|
| **<3.5** | 24 | 28.24 |
| **3.5-5.5** | 35 | 41.18 |
| **>5.5** | 26 | 30.59 |
| **TOTAL** | 85 | 100 |
| **MEAN ± SD= 4.50± 2.16** | | |

24 out of 85 patients had serum phosphorus value of < 3.5 mg/dl, 35 of them had value between 3.5mg/dl and 5.5mg/dl and in 26 patients value was > 5.5mg/dl.

**Table 5:** Distribution of subjects based on intact Parathyroid hormone levels.

| iPTH (in pg/ml) | Number | Percentage |
|---|---|---|
| **<100** | 26 | 30.59 |
| **100-150** | 9 | 10.59 |
| **150-300** | 19 | 22.35 |
| **300-600** | 24 | 28.24 |
| **>600** | 7 | 8.24 |
| **TOTAL** | 85 | 100 |
| **MEAN±SD=255.12±231.75pg/ml** | | |

Mean level of iPTH was 255.12±231.75 pg/ml with a range from 4.3 to 987.60pg/l. 36.48% of patients had intact PTH levels above 300pg/ml suggesting hyperparathyroidism as per K/DOQI guidelines. 22.35% of patients hadaccepted range (150-300 pg/ml) and 41.18% of patients had levels below 150pg/ml. 8.24% of patients had iPTH values > 600pg/ml and 30.59% of patients had iPTH levels less than 100pg/ml.

**Table 6:** Distribution of subjects based on 25OH vitamin D levels.

| 25 OH Vitamin D(ng/ml) | Number | Percentage |
|---|---|---|
| **≤20** | 45 | 52.94 |
| **21-29** | 17 | 20.00 |
| **≥30** | 23 | 27.06 |
| **TOTAL** | 85 | 100.00 |
| MEAN ±SD = 25.83±19.52 | | |

27.06 % of the patients had 25OH vitamin D levels of ≥ 30ng/ml, 52.94% of patients had vitamin D deficiency(≤20ng/ml) and 20% of patients had vitamin D insufficiency(21-29ng/ml).

**Table 7:** Distribution of subjects based on serum alkaline phosphatase levels.

| Alkaline Phosphatase ( U/L) | Number | Percentage |
|---|---|---|
| **<120** | 32 | 37.65 |
| **≥120** | 53 | 62.35 |
| **TOTAL** | 85 | 100 |
| **MEAN±SD=137.79±59.34** | | |

62.35 % had ALP value of ≥120U/L.

**Table 8:** Distribution of subjects based on the presence of Bone Mineral Disorders.

| Disorders | Number | Percentage |
|---|---|---|
| Hypercalcemia (>10.2mg/dl) | 5 | 5.88 |
| Hypocalcemia (<8.4 mg/dl) | 31 | 36.47 |
| Hyperphosphatemia ( >5.5mg/dl) | 26 | 30.59 |
| Hypophosphatemia ( <3.5mg/dl) | 24 | 28.24 |
| Hyperparathyroidism (>300pg/ml) | 31 | 36.48 |
| Hypoparathyroidism (<150pg/ml) | 9 | 10.59 |
| Patients with iPTH<100pg/ml | 26 | 30.59 |
| Patients with iPTH>600pg/ml | 7 | 8.24 |
| Serum alkaline phosphatase >120U/L | 53 | 62.35 |
| Vitamin D deficiency (≤ 20ng/ml) | 45 | 52.94 |
| Vitamin D insufficiency(21-29ng/ml | 17 | 20.00 |

The most was common mineral bone disorder was elevated serum alkaline phosphatase levels in 62.35% of patients, followed by vitamin D deficiency in 52.94%, hyperparathyroidism in 36.48%, hypocalcemia in 36.47%, hyperphosphatemia in 30.59% of patients. iPTH levels were <100pg/ml in 30.59% of our patients.

## Discussion

In our study the mean levels of serum corrected calcium was 8.71±1.09mg/dl. In a study by Ghosh et al., mean serum corrected calcium was 8.24±1.26mg/dl.[4] The results of our study showed

that only 47.06 % of patients had acceptable levels of serum corrected calcium, 36.47% had below and 16.47% had values above the acceptable levels. In the study done by Fatemeh Hayati et al., 55.4% had acceptable levels (8.4-9.5mg/dl), while 7.1% had above and 37.5% had values below acceptable levels, which is similar to our study.[1]

41.18% of patients in our study had acceptable levels of serum phosphorus between 3.5-5.5 mg/dl. Majority of patients had the values outside the acceptable levels, with 28.24% below and 30.59% above the acceptable levels. In the study by FatemehHayati et al., all the patients had serum phosphorus levels >5.5 mg/dl.[1]

In our study mean iPTH value was 255.12±231.75mg/dl. In Suresh Sankarasubbaiyyan et al.study, iPTH level was 124.6±174.9 pg/ml.[5] In Walter G. et al. study, mean levels of iPTH was 529±567pg/ml.[2]

41.8% of our patients had intact PTH levels <150pg/ml, 22.35% had between 150 to 300pg/ml and 36.48% of patients had more than 300pg/ml. Majority of our patients (77.66%) had iPTH levels outside the acceptable levels. In Study by Sanjay Vikrant et al., 53.1% of patients had hyperparathyroidism with iPTH levels >300pg/ml.[6] In our study 30.59% of patients had serum iPTHlevels<100pg/ml which is similar to study done by Salim Lim et al., in which 30% of patients had iPTH<100pg/ml.[7]

In our study, majority of patients (52%) had vitamin D deficiency. The study by Sanjay Vikrant et al., showed that 87% of patients had vitamin D deficiency.[6] The mean level of serum alkaline phosphatase in our study was 137.79±59.34 U/L. In Ghosh et al. study, mean levels of alkaline phosphatase were about 180U/L.[4]

A high prevalence of biochemical abnormalities of bone mineral metabolism was found in our study. 62.35% of patients had elevated alkaline phosphatase levels, 52.94% of patients had vitamin D deficiency, 41.18% of patients had iPTH levels <150pg/ml, 36.48% of patients had Secondary hyperparathyroidism with iPTH >300pg/ml, 36.47% of patients had hypocalcemia, 30.59% of patients had iPTH levels <100pg/ml, 30.59% of patients had hyperphosphatemia, 5.88% of patients had hypercalcemia.

Agarwal et al. found hypocalcemia in 49.6% of patients.[8] Prevalence of secondary hyperparathyroidism in our study was 36.48%. Agarwal et al. found hyperparathyroidism in 39.4% of patients similar to our study.[8] 30.59% of our patients had iPTH <100pg/ml with more predilection for adynamic bone disease. In Suresh Sankarasubbaiyyan et al., study, 69.5% of patients had iPTH levels less than twice the normal range (<130pg/ml).[5]

Limitations of our study include the small sample size, cross-sectional methodology, overrepresentation of male patients. In addition, there was no documentation of dialysis adequacy in the study population and other markers of bone disease like bone histology.

To conclude, our study found a spectrum of mineral and bone disorders in patients with chronic kidney disease stage 5 on maintenance hemodialysis. Mean levels of phosphate, corrected calcium and calcium phosphorus product were in the acceptable levels in our study population. We also found many patients with vitamin D deficiency, secondary hyperparathyroidism, oversupression of iPTH, hypocalcemia, hyperphosphatemia in our dialysis patients.

Two fifth of patients (40%) had over-suppression of iPTH levels and a third of our patients on maintenance hemodialysis were at risk of developing adynamic bone disease.

We found a lower prevalence rate (36%) of secondary hyperparathyroidism in our study population.

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