

Original Research Article

Study of prevalence of secondary hyperparathyroidism in chronic renal failure in Hadoti region, India

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ABSTRACT

Background: Secondary hyperparathyroidism is known and early complication of chronic renal failure patients. Aim of this study was to assess the prevalence of secondary hyperparathyroidism and correlation between serum parathyroid hormone level with biochemical parameters in renal failure patients in tertiary care hospital in Kota, Rajasthan.

Methods: A cross sectional observational study was carried out in 50 patients who had creatinine clearance of 30ml/min/1.73m² or less for greater than 6 weeks attended the OPD of department of General Medicine, New Medical College hospital, Kota, Rajasthan from May 2018 to November 2018. Investigations like complete blood count, renal function test, urine routine microscopy and USG abdomen with serum parathyroid hormone, serum phosphorus, serum calcium levels were done. Serum parathyroid hormone level was done by calorimetric method.

Results: The prevalence of secondary hyperparathyroidism in our study was 72%.

In hyperparathyroidism patient's serum calcium level was low and the difference was highly significant ($p < 0.001$). There is negative correlation between S.PTH and S. calcium level ($r = -0.536$). Mean serum calcium level in our study is 1.6mmol/l. In hyperparathyroidism patient's serum phosphate level was high and the difference was highly significant ($p < 0.001$). There was positive correlation between S.PTH and S.PO4 level ($r = 0.402$). Mean serum phosphorus level in our study is 5.7 mg/dl. Prevalence of hyperparathyroidism was high among CRF patients with normal BP than hypertensive patients and with normal sugar than diabetics but the difference in proportion was not significant ($p = 0.87$, $p = 0.98$ respectively). 90% patients were on haemodialysis while 10% patients were on conservative management.

Conclusions: Early detection of secondary hyperparathyroidism in chronic renal failure patients can reduce its complications like bone fracture and cardiovascular complications.

Keywords: Renal failure, Secondary hyperparathyroidism, Serum parathyroid hormone

INTRODUCTION

Chronic renal failure (CRF) refers to an irreversible deterioration in renal function, which classically develops over a period of years. Chronic kidney disease (CKD) is defined as functional abnormalities of the kidney lasting

longer than 3 months, with or without reduced glomerular filtration rate. It can also be defined by the presence of urinary albumin with an excretion rate higher than 300 mg/24 h or in a ratio of more than 200 mg of albumin to 1 g of creatinine.¹ The prevalence of CKD, in India ranges from 0.79% to 1.4%.² Initially CKD is without specific

symptoms and is generally only detected as an increase in serum creatinine or protein in the urine.³

Secondary hyperparathyroidism is a common complication of chronic kidney disease (CKD), and is characterized by elevated levels of serum parathyroid hormone (PTH) and abnormalities in bone and mineral metabolism. Initially, the elevated PTH levels serve to increase renal phosphorus excretion. However, as the GFR declines further, serum phosphorus levels start to rise and induce hypocalcemia by binding bioavailable calcium as CaHPO_4 , which indirectly leads to a further rise in PTH production. CKD also leads to decreased activity of 1- α -hydroxylase, thereby decreasing 1, 25-OH vitamin D. A lack of 1, 25-OH vitamin D inhibits gastrointestinal absorption of calcium and also directly stimulates the parathyroid glands.⁴ In CKD, chronic stimulation of the parathyroid gland's triggers diffuse polyclonal hyperplasia. As the chronic stimulation of CKD continues, the parathyroids begin to develop monoclonal nodules within a background of parathyroid hyperplasia. These nodules demonstrate increased resistance to vitamin D and calcimimetic medications and may be the etiology of the loss of negative feedback seen in 3^o HPT.^{5,6}

Renal hyperparathyroidism leads to a host of bone and cardiovascular problems that ultimately can cause fractures, decreased quality of life, and an increased risk of death.

The exact prevalence of secondary hyperparathyroidism in chronic haemodialysis patient is not known.

Secondary hyperparathyroidism develops early in the course of chronic renal insufficiency, even at the glomerular filtration rate (GFR) of 50-80mL/min/1.73m².⁷

The Kidney Disease: Improving Global Outcomes guidelines recommend that screening and management of renal hyperparathyroidism be initiated for all patients with chronic kidney disease stage 3 (estimated glomerular filtration rate, < 60 mL/min/1.73 m²). Since the 1990s, improving medical management with vitamin D analogs, phosphate binders, and calcimimetic drugs has expanded the treatment options for patients with rHPT, but some patients still require a parathyroidectomy to mitigate the sequelae of this challenging disease. The aim of this study is to estimate the prevalence of secondary hyperparathyroidism among patients with chronic renal failure who are on haemodialysis or conservative management attending OPD and admitted in New Medical College and Hospital, Kota (Rajasthan).

METHODS

A hospital based cross-sectional descriptive study was carried out 1st January 2018 to 30st June 2018 to find out

the prevalence of secondary Hyperparathyroidism in chronic renal failure patients.

Sample size

After getting approved from the institutional research review board plan of study was executed in the field. ALL patients having chronic renal failure (creatinine clearance of <30ml/min/1.73m² for greater than 6 week) and age above 12 years, admitted or attending OPD of New medical college & Hospital, Kota were included. Patients with known condition of parathyroid gland disease or malignancy or bone disease were excluded. 50 patients were selected. A detailed history and physical examination were carried out. All the patients underwent routine investigations including CBC, blood sugar, kidney function tests, serum sodium and potassium, lipid profile, serum ionized calcium, serum phosphorus, urine examination, ultrasound abdomen and kidney, ECG, x-ray. Serum parathyroid level was measured by colorimetric method.

Creatinine clearance was calculated using following formula:

Creatinine Clearance (ml/min) = $140 - \text{age} \times \text{Ideal body weight in kg} / 72 \times \text{Serum Cr (mg/dl)}$ (x 0.85 for women).

Serum parathyroid hormone level 8-51pg/ml was considered as normal.⁸

Statistical analysis

Data thus collected were entered in Microsoft excel 2010 Worksheet in the form of master chart. Qualitative data were expressed in the form of percentage and proportions. Quantitative data were expressed in the form of Means and Standard Deviations. The comparison between proportions was assessed by Chi-square Test. P-value of 0.05 or less was interpreted as significant for the analysis.

The study protocol, patient information sheet and consent form were approved by institutional Ethical Committee.

RESULTS

Total 50 patients were included in study. Out of these 50 patients 28 were males and 22 were females. Mean age of males was 48.6 year and mean age of females was 45.9 year. (Table 1).

Table 1: Distribution of patients age according to sex.

Age	Male (in years) (N=28)	Female (in years) (N=22)
Minimum age	16	15
Maximum age	73	67
Mean age	48.6	45.9

Maximum patients of chronic renal failure (CRF) were in 51 to 60 year age group (30%) and 41 to 50 year age group (28%). Minimum patients were of 71 to 80 years age group. (Table 2). Chief presenting complaints were breathlessness (42%), decrease urine (26%), pedal edema (26%), convulsions (4%) and left ventricular failure (2%). Hypertension was the most common (62%) underlying disease among CRF patients followed by nephrotic syndrome (22%), Diabetes (16%), hepatitis C (12%) (Table 3).

Total 45 patients of CRF were on haemodialysis out of which 71% had high PTH level, 5 were not on haemodialysis out of which 80% had high PTH level.

Prevalence of secondary hyperparathyroidism (PTH >51 pg/dl) was in 36 patients (72%) and 14 patients showed PTH level less than 51 pg/dl. (Table 4).

Table 2: Distribution of CRF patients according to age groups.

Age	Number of patients	% of patients
11-20	3	6%
21-30	7	14%
31-40	2	4%
41-50	14	28%
51-60	15	30%
61-70	7	14%
71-80	2	4%
Total	50	100

Serum parathyroid mean level was 99.68 pg/dl±72.6 pg/dl. Serum calcium mean level was 1.69 mmol/L±0.58 mmol/L.

Table 3: Distribution of CRF patients according to underlying disease.

Underlying disease	Number of patients	% of patients
Hypertension	31	62%
Nephrotic syndrome	11	22%
Diabetes mellitus	8	16%
Hepatitis C	6	12%
RA	4	8%
Hypothyroidism	1	2%
Pulmonary TB	1	2%
CVA	1	2%
APKD	1	2%

Table 4: Distribution of CRF patients according to serum PTH level.

Level of PTH	Number of CRF Patients (%)
PTH <51 pg/dl	14 (28%)
PTH >51 pg/dl (Hyperparathyroidism)	36 (72%)

Serum phosphate mean level was 5.8±1.6. Serum urea mean level was 120.1 mg/dl±20.6 mg/dl. Serum creatinine mean level was 7.2 mg/dl±2.2 mg/dl. Creatinine clearance mean level was 4.9±1.8 (Table 5).

Hyperparathyroidism was high among CRF patients with normal BP than hypertensive patients and with normal sugar than diabetics but the difference in proportion was not significant (p= 0.87, p= 0.98 respectively). (Table 6, 7).

Table 5: Measurement of various serum markers in CRF patients.

Parameter	Mean	Standard Deviation	Min.	Max.
S. PTH (pg/ml)	99.68	72.6	14.5	350
S. Calcium (mmol/L)	1.69	0.58	0.20	2.60
S. PO4(mg/dl)	5.8	1.6	2.2	9.2
S. Urea (mg/dl)	120.1	20.6	60	154
S. creatinine (mg/dl)	7.2	2.2	2.8	9.9
Creatinine clearance (ml/min.)	4.9	1.8	1.4	10.1

Table 6: Distribution of PTH level according to blood pressure of CRF patients.

Blood pressure	CRF patients with Normal PTH (<51 pg/dl)		CRF patients with high PTH (>51 pg/dl)		Total	
	No.	%	No.	%	No.	%
CRF Patients with Normal BP	5	26.3%	14	73.7%	19	
CRF Patients with Hypertension	9	29.0%	22	71.0%	31	
Total	14	28%	36	72%	50	

Chi-square= 0.024 with 1 degree of freedom; p= 0.87, LS:NS.

Table 7: Distribution of PTH level according to blood sugar of CRF patients.

Blood sugar	CRF patients with Normal PTH (<51 pg/dl)		CRF patients with high PTH (>51 pg/dl)		Total
	No.	%	No.	%	
CRF Patients with normal blood sugar	11	26.9%	30	73.1%	41
CRF Patients with diabetes	3	33.3%	6	66.7%	9
Total	14	28%	36	72%	50

Chi-square= 0.0001 with 1 degree of freedom; p= 0.98 LS: NS.

Table 8: Distribution of serum calcium level according to serum PTH level in CRF patients.

S. PTH level	Patients with Normal S. Calcium (mmol/L)		Patients with Low S. Calcium (mmol/L)		
	Mean	SD	Mean	SD	
CRF patients with Normal PTH (<51 pg/dl) (N=14)	2.4 (n=12)	0.4	2.1 (n=2)	0.3	
CRF patients with high PTH (>51 pg/dl) (n=36)	2.2 (n=3)	0.3	1.6 (n=33)	0.3	t=3.31 p=0.002

Table 6 shows that hyperparathyroidism was slightly high among CRF patients with normal BP than hypertensive patients but the difference in proportion was not significant.

Table 7 shows that hyperparathyroidism was high among CRF patients with normal blood sugar than diabetics but the difference in proportion was not significant. In hyperparathyroidism patient’s serum calcium level was low and the difference was highly significant (p<0.001) (Table 8).

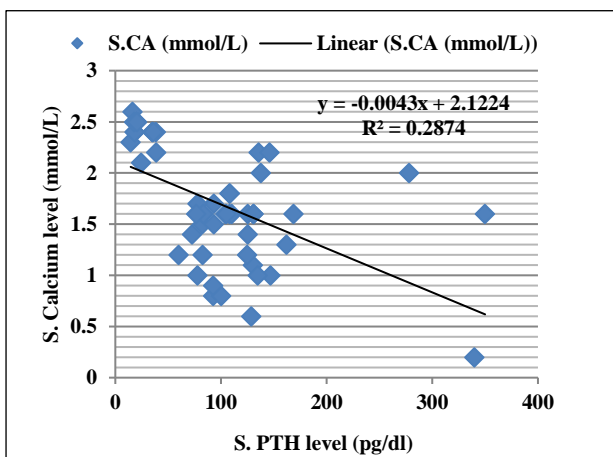


Figure 1: Correlation of S.PTH and S. phosphate level in hyperparathyroidism patients.

Correlation graph of serum PTH and serum calcium levels in hyperparathyroidism patients shows that there is negative correlation between them. As S. PTH level increases, s. calcium level decreases. Correlation coefficient (r) value is -0.536 that means there is strong level negative correlation (Figure 1).

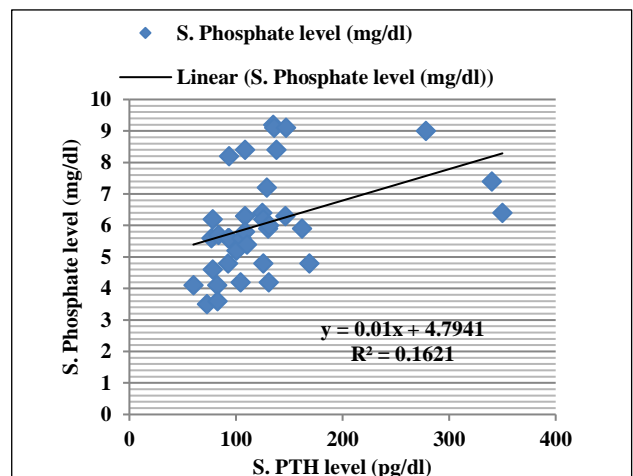


Figure 2: Correlation of S. PTH and S. Phosphate levels in hyperparathyroidism patients.

In hyperparathyroidism patient’s serum phosphate level was high and the difference was highly significant (p<0.001). (Table 9)

Correlation graph of serum PTH and serum phosphate levels in hyperparathyroidism patients shows that there is positive correlation between them. As S. PTH level increases, s. phosphate level also increases. Correlation coefficient (r) value is 0.402 that means there is moderate level positive correlation (Figure 2).

DISCUSSION

A hospital based cross-sectional descriptive study was carried out to find out the prevalence of secondary Hyperparathyroidism in chronic renal failure patients. It is one of the leading causes of chronic morbidity and

mortality worldwide. This cross-sectional study consists of 50 patients admitted in new hospital medical college District Kota, Rajasthan. Author studied the prevalence

of secondary hyperparathyroidism in chronic renal failure patients and correlation with serum phosphate and serum calcium.

Table 9: Distribution of serum phosphate level according to serum PTH level in CRF patients.

S. PTH level	Patients with Normal S. PO4 (mg/dl)		Patients with high S. PO4 (mg/dl)		
	Mean	SD	Mean	SD	
CRF patients with Normal PTH (<51 pg/dl) (n=14)	3.2 (n=11)	0.4	4.5 (n=3)	0.4	
CRF patients with high PTH (>51 pg/dl) (n=36) (n=36)	4.2 (n=4)	0.3	5.7 (n=32)	0.4	t= -7.21 p<0.001

In this study it was observed that maximum patients of chronic renal failure (CRF) were in 51 to 60 year age group (30%) and 41 to 50 year age group (28%). Minimum patients were of 71 to 80 years age group. Minimum and maximum age of male patients was 16 and 73 year respectively.

In female patients maximum and minimum age were 15 and 67 year. Mean age of males was 48.6 year and mean age of females was 45.9 year. This age group was similar to Agarwal SK et al, and Ghosh B et al, studies.^{9,10} In this study out of total 50 patients 58.3% were males and 41.6% were females which is similar to the study done by Jalalzadeh M et al, in this study out of 50 patients 36 patients (72%) had elevated level of parathyroid hormone that similar to other study by Jalalzadeh M et al, and Owda A et al, in this study Serum phosphorus level were elevated (5.8mg/dl) that are supported by study of Jalalzadeh M et al, (6.5mg/dl) and Mejia Pinedea et al, 1 (5.66mg/dl).¹¹⁻¹³ In this study Serum calcium level were decreased (1.69mmol/L) that are supported by study of Jalalzadeh et al, (2.19mmol/L), Mejia Pinedea A et al, (2.20mmol/L), E1 Desoky S et al, (1.9mmol/L).^{11,13,14}

In this study prevalence of secondary hyperparathyroidism in diabetic patients is 66% and in non-diabetic patients is 73%, that is supported by other study by Arevalo-lorido JC et al, in their study on 407 patients (214 diabetics) hyperparathyroidism was found in 60.4% of diabetic patient's vs 65% of non-diabetic patients.¹⁵ This observation is also supported by Owda A et al, in their study there was no significant difference in serum PTH levels between diabetic and non-diabetic patients.¹²

CONCLUSION

Out of 50 patients in 36 patients author found higher level of serum parathyroid. Hence the prevalence of secondary hyperparathyroidism in this study is 72%.

In this study out of 36 patients of secondary hyperparathyroidism 58% of patients (21) were male and 42% of patients (13) were female. Maximum patients were between 40 to 60 years of age group.

The common presentation of patients was breathlessness (42%) followed by pedal oedema (26%), decrease urine output (26%), convulsion (4%) and LVF (2%).

Hypertension was most common cause of nephropathy in this study (62%) followed by nephrotic syndrome (22%), diabetic nephropathy (16%), hepatitis C (12%), connective tissue disease (8%) and tuberculosis (2%).

In hyperparathyroidism patient's serum phosphate level was high and the difference was highly significant (p<0.001). Apart from this there is positive correlation between S.PTH and S.PO4 level that suggest higher level of S. PO4 is associated with higher level of S.PTH. Mean serum phosphorus level in this study is 5.7 mg/dl.

In hyperparathyroidism patient's serum calcium level was low and the difference was highly significant (p<0.001). There is negative correlation between S.PTH and S. calcium level suggesting that lower S. Ca level is associated with higher level of S.PTH. Mean serum calcium level in this study is 1.6mmol/l.

90% patients were on haemodialysis while 10% patients were on conservative management. Patients who are on haemodialysis are mostly stage 5 CKD. So declining kidney function associated with higher level of parathyroid hormone. By early management of declining renal function, we can prevent or control secondary hyperparathyroidism.

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Conflict of interest: None declared

Ethical approval: Not required

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