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Clinical And Biochemical Profile of Secondary Hyperparathyroidism in Chronic Renal Failure Patients at Tertiary Care Hospital

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Abstract

Background: secondary hyperparathyroidism is known and early complication of chronic renal failure patients

Aim: To assess clinical and biochemical profile 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, Kota, Rajasthan from May 2018 to November 2018. Investigations like complete blood count, blood sugar, renal function test, urine routine microscopy and USG whole 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%. The common presentation of patients were breathlessness (42%) followed by pedal oedema (26%), decrease urine output (26%), convulsion (4%) and LVF (2%).In hyperparathyroidism patients 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 patients serum phosphate level was high and the difference was highly significant ($p<0.001$). There was positive correlation between S.PTH and s. phosphorus 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.

Conclusion: 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 kidney failure is a slow progressive loss of kidney function over a period of several 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. This serious disorder arises from disturbances in the regulation of the intracellular and extracellular levels of PTH, calcium, phosphorus and vitamin D (calcitriol), which become more severe as kidney function declines. Secondary hyperparathyroidism developsearly in the course of chronic renal insufficiency, even at theglomerular filtration rate (GFR) of 50-80mL/min/1.73m2.[4] Patients with rHPT experience increased rates of cardiovascular problems and bone disease. The Kidney Disease: Improving Global Outcomes guidelines recommend that screening and management of rHPT be initiated for all patients with chronic kidney disease stage 3 (estimated glomerular filtration rate, < 60 mL/min/1.73 m^2). An increase in PTH levels typically develops when the glomerular filtration rate (GFR) drops below 60 mL/min/1.73 m^2.[5]

Abnormalities in serum levels of phosphorus and calcium tend to occur much later in the course of CKD (typically when the GFR drops below 40 mL/min/1.73 m^2).[6] 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.[7]

In CKD, chronic stimulation of the parathyroid glands 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° HPT [8,9]. rHPT is a common complication of CKD that stems from hypocalcemia, reduced bioactivity of vitamin D, and elevated levels of FGF-23. rHPT 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 aim of this study is to study the clinical and biochemical profile of secondary hyperparathyroidism among patients with chronic renal failure who are on hemodialysis or conservative management attending OPD and admitted in New Medical College and Hospital, Kota (Rajasthan).

Material & Methods

A hospital based cross-sectional descriptive study was carried out 1st January 2018 to 30st June 2018 to find out clinical and biochemical profile 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 was carried out. All the patients underwent routine investigations including CBC, blood sugar, kidney function tests, serum sodium and potassium, lipid profile, serum ionised 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 – age x Ideal body weight in kg/72 x Serum Cr (mg/dl) (x 0.85 for women) Serum parathyroid hormone level 8-51pg/ml was considered as normal.[10]

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 & Discussion

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

S. No.	Age	Male (in years) (n=28)	Female (in years) (n=22)
1	Minimum age	16	15
2	Maximum age	73	67
3	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)

Table 2

S.No.	Age	Number of patients	% of patients
1	11-20	3	6%
2	21-30	7	14%
3	31-40	2	4%
4	41-50	14	28%
5	51-60	15	30%
6	61-70	7	14%
7	71-80	2	4%
	Total	50	**100**

Chief presenting complaints were breathlessness (42%), decrease urine (26%), pedal edema (26%), convulsions (4%) and left ventricular failure (2%). (Table 3)

Table 3

S. no.	Chief complaints	Number of CRF patients (%)
1	Breathlessness	21(42%)
2	Decreased urine	13 (26%)
3	Pedal edema	13 (26%)
4	Convulsion	2 (4%)
5	LVF	1 (2%)

Table no. 3 shows that major complaint was breathlessness (in 42% patients) and least complaint was LVF (in 2% patients).

Hypertension was the most common (62%) underlying disease among CRF patients followed by nephrotic syndrome (22%), Diabetes (16%), hepatitis C (12%) (Table 4)

Table 4

S. no.	Underlying disease	Number of patients	% of patients
1	Hypertension	31	62%
2	Nephrotic syndrome	11	22%
3	Diabetes Mellitus	8	16%
4	Hepatitis C	6	12%
5	RA	4	8%
6	Hypothyroidism	1	2%
7	Pulmonary TB	1	2%
8.	CVA	1	2%
9.	APKD	1	2%

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 5)

Table 5

S. No.	Level of PTH	Number of CRF Patients (%)
1	PTH <51 pg/dl	14 (28%)
2	PTH >51 pg/dl (Hyperparathyroidism)	36 (72%)

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. 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 6)

Table 6

S. no.	Parameter	Mean	Standard Deviation	Min.	Max.
1	S. PTH (pg/ml)	99.68	72.6	14.5	350
2	S. Calcium (mmol/L)	1.69	0.58	0.20	2.60
3	S. PO4(mg/dl)	5.8	1.6	2.2	9.2
4	S. Urea (mg/dl)	120.1	20.6	60	154
5	S. creatinine (mg/dl)	7.2	2.2	2.8	9.9
6	Creatinine clearance (ml/min.)	4.9	1.8	1.4	10.1

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 7, 8)

Table 7

Distribution of PTH level according to blood pressure of CRF patients

S. no.	Blood pressure	CRF patients with Normal PTH (<51 pg/dl)		CRF patients with high PTH (>51 pg/dl)		Total
		No.	%	No.	%	
1	CRF Patients with Normal BP	5	26.3%	14	73.7%	19
2	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 no. 7 shows that hyperparathyroidism was slightly high among CRF patients with normal BP than hypertensive patients but the difference in proportion was not significant.

Table 8

Distribution of PTH level according to blood sugar of CRF patients

S. no.	Blood sugar	CRF patients with Normal PTH (<51 pg/dl)		CRF patients with high PTH (>51 pg/dl)		Total
		No.	%	No.	%	
1	CRF Patients with Normal blood sugar	11	26.9%	30	73.1%	41
2	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 no 8 shows that hyperparathyroidism was high among CRF patients with normal blood sugar than diabetics but the difference in proportion was not significant.

In hyperparathyroidism patients serum calcium level was low and the difference was highly significant ($p<0.001$). (Table 9)

Table 9

S. no.	S. PTH level	Patients with Normal S. Calcium (mmol/L)		Patients with Low S. Calcium (mmol/L)		
		Mean	SD	Mean	SD	
1	CRF patients with Normal PTH (<51 pg/dl) (N=14)	2.4 (n=12)	0.4	2.1 (n=2)	0.3	
2	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

In hyperparathyroidism patients serum phosphate level was high and the difference was highly significant ($p<0.001$). (Table 10)

Table 10

S. no.	S. PTH level	Patients with Normal S. PO4 (mg/dl)		Patients with high S. PO4 (mg/dl)		
		Mean	SD	Mean	SD	
1	CRF patients with Normal PTH (<51 pg/dl) (n=14)	3.2 (n=11)	0.4	4.5 (n=3)	0.4	
2	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

Discussion

A hospital based cross-sectional descriptive study was carried out to find out the clinical and biochemical profile of secondary Hyperparathyroidism in chronic renal failure patients. It is one of the leading cause of chronic morbidity and mortality worldwide.

This cross-sectional study consists of 50 patients admitted in new hospital medical college District Kota, Rajasthan.

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 (2005)[11] and Ghosh B et al (2010)[12] studies. In our 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[13].

In this study out of 50 patients 36 patients (72%) had elevated level of parathyroid hormone that similar to other study by JalalzadehM et al[13] and OwdaA et al[14].In this study Serum phosphorus level were elevated(5.8mg/dl) that are supported by study ofJalalzadeh M et al[13](6.5mg/dl) and Mejia Pinedea et al[15](5.66mg/dl). In this studySerum calcium level were decreased (1.69mmol/L) that are supported by study of Jalalzadeh et al[13] (2.19mmol/L), Mejia PinedeaA et al[15] (2.20mmol/L), E1 Desoky S et al[16] (1.9mmol/L).

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[17].In their study on 407

patients (214 diabetics) hyperparathyroidism was found in 60.4% of diabetic patients vs 65% of non-diabetic patients. This observation is also supported by OwdaA et al[14]. In their study there was no significant difference in serum PTH levels between diabetic and non-diabetic patients.

Conclusion

Out of 50 patients in 36 patients we found higher level of serum parathyroid. Hence the prevalence of secondary hyperparathyroidism in our 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 were breathlessness (42%) followed by pedal oedema (26%), decrease urine output (26%), convulsion (4%) and LVF (2%).

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

In hyperparathyroidism patients 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 our study is 5.7 mg/dl.

In hyperparathyroidism patients 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 our 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.

Abbreviations

LVF – Left ventricular failure

PTH – Parathyroid hormone

CRF – Chronic renal failure

CKD – Chronic kidney disease

GFR – Glomerular filtration rate

rHPT – renal hyperparathyroidism

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