ORIGINAL ARTICLE

Intact Parathyroid Hormone Level in Different Stages of Chronic Kidney Disease

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Abstract:

Secondary hyperparathyroidism is the first and most recognizable complication of chronic kidney disease (CKD) because parathyroid hormone (PTH) plays a compensatory role to maintain calcium and phosphate homeostasis. Progressive renal failure give rise to a steady increase in parathyroid hormone concentration, which is related to occurrence of renal bone disease. The objective of this study was to find out the intact parathyroid hormone level in different stages of chronic kidney disease patients. This cross sectional study was carried out in the department of physiology, Dhaka Medical College from January to December 2009. 100 chronic kidney disease patients aged 20 to 60 years were selected as experimental group and 20 apparently healthy subjects were in control group and were matched for age and body weight. Patients were divided into three stages based on their creatinine clearance rate (Ccr). Group B_1 includes 34 patients marked as stage II with Ccr 60-89 ml/min, Group B_2, Group B_3 consists of 36 and 30 patients each and marked as stage III and stage IV with Ccr 30-59 ml/min and 15-29 ml/min respectively. Intact PTH was measured by chemiluminescent immuno assay method. Statistical analysis was done by unpaired Student's "t"- test and pearson's correlation test. Mean serum PTH level was significantly higher in all experimental groups than that of control group ($p< 0.001$). High level of PTH was found in 74% patients in stage II, 81% in stage III and 97% patients in stage IV. Again, a significant negative correlation of parathyroid hormone with Ccr was observed in patients with CKD in all three stages. From the findings of the present study it may be concluded that intact PTH level progressively increases from early stage to late stage of chronic kidney disease.

Introduction:

Renal diseases are the vital issue in health service delivery system. There are increasing numbers of patients of chronic kidney disease worldwide. About 85% of world population lives in low income or middle income countries where number of chronic kidney disease is highest. In Bangladesh about 8 to 10 million peoples are suffering from some form of renal diseases, among them 15 – 20 thousands patients develop chronic kidney diseases and end stage renal diseases[1].

Chronic kidney disease (CKD) is an irreversible deterioration of renal function which develops over the period of months or

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years[2]. CKD may be caused by any condition which destroys the normal structure and functions of the kidneys. The loss of excretory, metabolic and endocrine functions of the kidneys decreases capability of the kidneys to excrete waste products. On the basis of GFR (glomerular filtration rate), chronic kidney disease can be classified into five stages - Stage I- Kidney damage with normal or relatively high GFR (>90 ml/min/1.73 m^2 bsa), Stage II – Kidney damage with mildly reduced GFR (60-89 ml/min/1.73m^2 bsa), Stage III - Moderately reduced GFR (30-59 ml/min/1.73 m^2 body surface area), Stage IV - Severely reduced GFR (15-29 ml/min/1.73 m^2 body surface area), Stage V - Established kidney failure (GFR <15 ml/min/1.73 m^2 body surface area)[3].

In CKD several biochemical and hormonal abnormalities occur. Minerals and bone disorders that are related to CKD includes abnormalities in phosphate retention, hypocalcaemia, hyperparathyroidism, increased alkaline phosphatase level and abnormalities in bone turnover[4].

Parathyroid hormone is one of the essential hormone which acts as a key controller of calcium and phosphate metabolism. If there is any abnormalities in PTH secretion, calcium and phosphate homeostasis is deranged[5].

Secondary hyperparathyroidism is the first and most important complication in chronic kidney disease because PTH secretion is a compensatory mechanism to maintain calcium and phosphate level within physiological ranges[6]. Decreased creatinine clearance rate tends to rise PTH secretion. Moreover long term consequences of hyperparathyroidism are renal osteodystrophy, soft tissue calcification particularly blood vessels, immune dysfunction, and anaemia[7].

Therefore, the present study was designed to assess the serum PTH (intact) level in different stages of CKD and to utilize the out come of the study as background information for the physicians for better management of the CKD patients. Also PTH measurement is essential to create awareness among the clinicians and CKD patients about the effects of hyperparathyroidism.

Materials and method:

The cross sectional study was carried out in the department of physiology, Dhaka medical college, Dhaka during the period from January to December 2009. A total number of 120 male and female with age ranging from 20 to 60 years were included in the study. Among them 20 apparently healthy subjects were considered as control (group A) and 100 were diagnosed chronic kidney disease patient were taken in experimental group (group B) in their various stages of kidney disease. Stages are designated by the severity of the disease - stages : II (mild) , stage III (moderate) & stage IV (severe). Group B was again subdivided into group B_1, B_2 and B_3 on the basis of creatinine clearance rate (Ccr). Group B_1 consisted of 34 patients in stage II with Ccr 60 – 89 ml / min. Similarly Group B_2 and B_3 consisted of 36 and 30 patients in stage III and stage IV with Ccr 30 – 59 ml /min and 15 – 29 ml /min respectively[3].

The experimental subjects were selected from the nephrology OPD of Holy Family Red Crescent Hospital and control subjects were selected from the Dhaka city by personal contact. Patient with history of acute renal failure, patient taking vitamin D preparation or calcium supplement previously, patient with nephrotic range proteinuria, patient with liver disease were excluded. All ethical consideration

for the subjects was taken into account before inclusion into the study. The aims and benefits of the study were explained to each subject and informed consent was taken. With all aseptic preparation 5.0 (five) ml of fasting venous blood was collected. Serum was prepared and send to the laboratory of immunology department in Bangabandhu Sheikh Mujib Medical University. Serum PTH was measured by chemiluminescent immuno assay method [8,9]. Data was expressed as mean ± SD. Statistical analysis was done by unpaired Student's 't' test and Pearson's correlation test as applicable.

Results:

The demographic data of the study subjects are shown in Table I. Subjects of all groups were well matched for age and body weight. Parathyroid hormone level in control group were within the normal range. Mean serum intact PTH levels were significantly higher in group B_1, B_2, B_3 than that of group A. Again, this value was progressively higher in B_2 than B_1 and B_3 than B_2 (Table II). Figure 1 presented the distribution of high PTH levels in different stages of kidney disease. The cutoff point of PTH level is > 55 pg /ml [10]. In stage II (B_1) out of 34 patients, 25 (73.5%) , in stage III (B_2) out of 36 patients 29 (80.55%), in stage IV (B_3) out of 30 patients 29 (96.7%) were hyperparathyroids. No patients were hypoparathyroid. Creatinine clearance rate showed significant ($p < 0.001$) negative correlation with PTH (Figure 2).

Table I : Age and body weight in different study groups (n =120)

Groups	Age (mean ± sd)	Body weight
A (n=20)	39.45 ± 08.09	65.85 ± 6.84
B_1 (n=34)	35.41 ± 10.15	65.09 ± 7.88
B_2 (n=36)	38.22 ± 09.57	66.92 ± 7.17
B_3 (n=30)	43.87 ± 10.71	65.87 ± 6.83

Table –II : Creatinine clearance rate and Parathyroid hormone in different study groups (n =120)

Groups	Creatinine clearance rate	Parathyroid hormone
A (n=20)	98.64 ± 26.11	40.60 ± 10.44
B_1 (n=34)	55.71 ± 08.68	79.11 ± 19.99
B_2 (n=36)	38.19 ± 06.56	105.89 ± 37.22
B_3 (n=30)	20.14 ± 04.11	220.10 ± 127.18

Statistical analysis

Groups	p value	Groups	p value
A vs B_1	0.001**	A vs B_2	0.015*
A vs B_3	0.007**	B_1 vs B_2	0.529 ns
B_1 vs B_3	0.01*	B_2 vs B_3	0.01*

A = Apparently healthy control group p*** = Highly significant
B_1 = Stage II CRF B_2 = Stage III CRF B_3 = Stage IV CRF

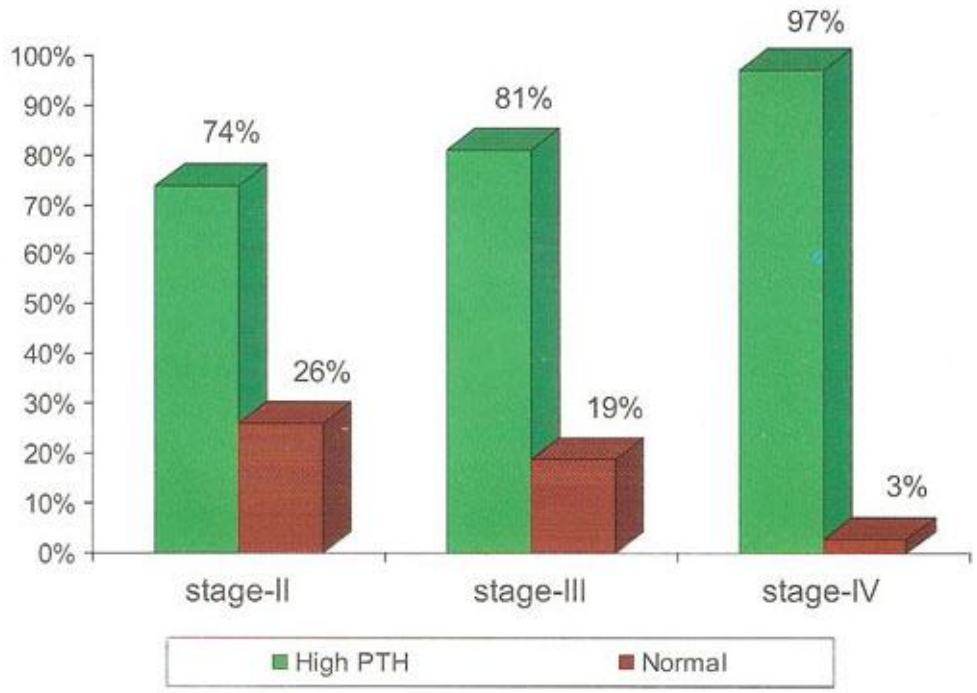

Figure 1: Distribution of high PTH level in different experimental groups (n=100)

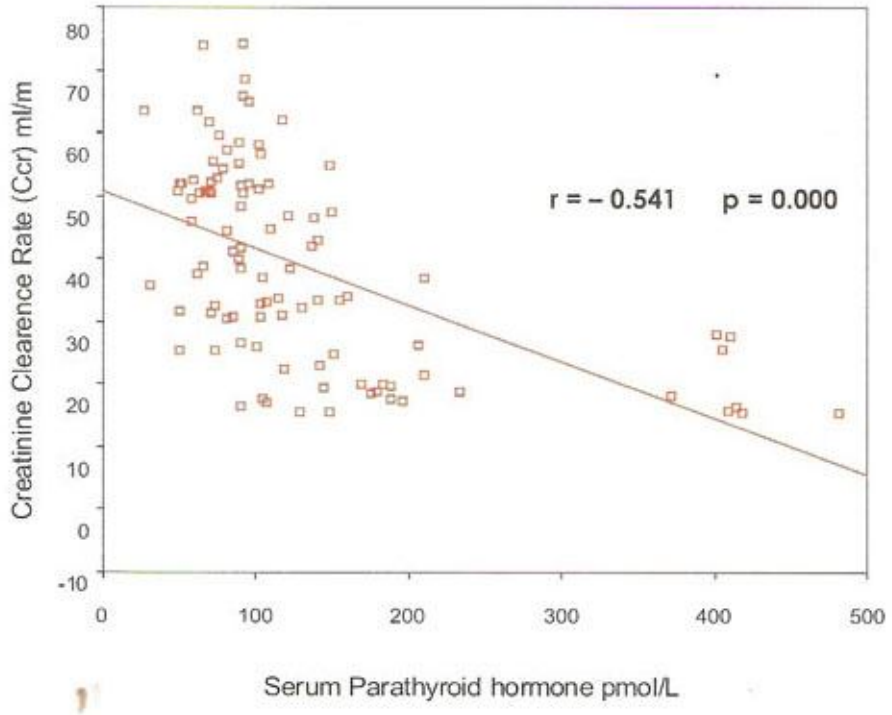

Figure 2: Correlation between PTH and CCr in experimental group (n = 100)

Discussion :

Mean serum PTH level was significantly higher in all experimental groups than control group ($p< 0.001$). Again, markedly elevated level of PTH was found in 74% patients in stage II, 81% in stage III and 97% patients in stage IV. A significant negative correlation of parathyroid hormone with Ccr was observed in all patients with CKD. Again, PTH was studied in different stages of chronic kidney disease and progressive rise of this hormone level in different stages was found. Similar type of findings was reported by several authors [11-12].

Similarly, parathyroid hormone level in different stages of CKD was increased gradually and it was significantly higher in moderate to severe renal failure in other studies[13-16].

Results of the study showed that there was negative correlation of serum PTH with creatinine clearance rate. Similar type of findings was reported by some other investigators [17].

Secondary hyperparathyroidism also occur in graded renal failure of an experimental rat[17]. In several studies it was observed that in patients with chronic kidney diseae develop secondary hyperparathyroidism It was suggested that hypocalcaemia, low calcitriol level and phosphorus retention are the key factors in the pathogenesis of secondary hyperparathyroidism[18]. Increased PTH level in all the experimental groups may be due to hyperphosphataemia, decreased calcium absorption and impaired 1,25 dihydroxy vitamin D_3 production.

From this study it may be concluded that the intact PTH secretion gradually increases in different stages of chronic kidney disease and is proportional to the severity of the chronic kidney diseases.

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