

BRIEF REPORTS

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Correlation of Serum Parathormone Level with Biochemical Parameters in Chronic Renal Failure

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A prospective study was carried out to assay the level of serum intact parathormone and its correlation with biochemical parameters in patients with chronic renal failure (CRF). The study included 64 children (44 with CRF, and 20 age and sex matched controls). Serum intact parathormone (iPTH), serum creatinine, urea, calcium, inorganic phosphate and alkaline phosphatase were estimated. Creatinine clearance (Ccr) was estimated by Schwartz formula. Patients with CRF were divided into four groups based on their Ccr (mild CRF with mean Ccr $59.17 \pm 1.18.53$ mL/min/1.73 m² (n = 6) moderate CRF with mean Ccr 34.98 ± 7.75 mL/min/1.73 m² (n = 7); severe CRF with mean Ccr 17.71 ± 5.40 mL/min/1.73 m² (n = 15); and end-stage renal disease with mean Ccr 6.46 ± 1.71 mL/min/1.73 m² (n = 16). Mean serum iPTH levels were 93.00 ± 46.62 pg/mL in CRF and 16.52 ± 9.35 pg/mL in controls. Groupwise mean serum (iPTH) levels were 48.50 ± 4.76 , 67.29 ± 7.91 , 82.42 ± 9.67 and 130.66 ± 58.74 pg/mL in mild, moderate, severe CRF and end-stage renal failure respectively. Mean serum iPTH level of CRF (93.00 ± 46.42 pg/mL) negatively correlated with mean Ccr (22.02 ± 18.53 mL/min/1.73 m²) ($P < 0.001$) and mean serum calcium (7.30 ± 1.02 mg/dL) ($P < 0.001$) and positively correlated with mean inorganic phosphate (5.76 ± 1.1 mg/dL) ($P < 0.05$) and mean alkaline phosphatase (355.14 ± 185.53 UL) ($P < 0.001$). We conclude that increased iPTH level occur even early in the course of CRF and progressive hypocalcemia and hyperphosphatemia are the initiating factors for the development of hyperparathyroidism.

Keywords: Chronic renal failure, Hyperparathyroidism, Parathormone

CHRONIC renal failure (CRF) produces a number of abnormalities of calcium and phosphorus metabolism. Secondary hyperparathyroidism develops early in the course of

chronic renal insufficiency(1), even at the glomerular filtration rate (GFR) of 50-80 mL/min/1.73 m²(2). It is generally thought to result from hypocalcemia as a result of

phosphate retention and deficient $1,25(\text{OH})_2\text{D}_3$ synthesis(3). In response to an increase in serum phosphorus concentration, production of $1,25(\text{OH})_2\text{D}_3$ is decreased and secretion of parathyroid hormone (PTH) is increased, which in turn increases urinary excretion of serum phosphorus to maintain normal serum calcium and phosphorus level. Therefore, PTH is an important factor in the regulation of calcium and phosphorus metabolism and the key target organ of parathormone action are the kidneys and skeleton(4). Without treatment the severity of secondary hyperparathyroidism generally worsens with progressive decline in renal function.

PTH is an 84-amino acid hormone which is metabolised into amino (1-34 amino acids) and carboxyl (53-84 amino acids) terminal fragments. Different radioimmunoassay for PTH assay either the intact, amino, carboxyl or mid region fragments shows inaccuracy (5,6), but immunochemilumino-metric assay (7) of intact PTH (iPTH) is accurate and was used in the present study.

In Bangladesh, data regarding PTH in relation to different biochemical parameters in children with CRF are not available. Therefore, this study was conducted to estimate iPTH levels in children with CRF in their different stages of presentation as well as in healthy control to find out its correlation with different biochemical parameters.

Subjects and Methods

This prospective case-control study was carried out in the Department of Pediatrics, Bangabandhu Sheikh Mujib Medical University, Dhaka, during May 2000 to May 2002. A total of 44 patients in different stages of CRF and 20 age and sex matched healthy controls were enrolled. Patient below 15 years of age with creatinine clearance $<75 \text{ mL}/\text{min}/1.73 \text{ m}^2$ were diagnosed to have CRF.

Children with acute renal failure were excluded from the study. The etiology and severity of CRF in these children was done by clinical, biochemical and imaging studies. Serum iPTH was assayed in the Department of Biochemistry, Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders, Dhaka.

For each case and control, 10 mL of morning blood sample was drawn from antecubital vein in a plain test tube. Morning sample was preferred because of the nocturnal rise in iPTH levels(7). For separation of serum, blood was first allowed to clot and then centrifuged at 2500 rpm for 5 minutes. For estimation of iPTH, serum was transferred to an airtight, capped glass container. Visibly hemolyzed samples were discarded. In case of necessity, serum was stored at $2-8^\circ\text{C}$ for up to 8 hours and in some cases of long delay, samples were stored at -20°C .

The entire iPTH assay procedure was done by Immulite analyzer. Immulite iPTH is a solid-phase, two-site chemiluminescent enzyme-labeled immunometric assay. For estimation of iPTH, reagent was collected from the Diagnostic Product Corporation (Los Angeles) (Lot No. PILKPP-5). The normal reference range of this procedure is $7-53 \text{ pg}/\text{mL}$ ($0.7-5.6 \text{ } \mu\text{mol}/\text{L}$).

In this study, intraassay and interassay coefficient variation could not be performed due to technical constraints, rather status of iPTH between cases and age and sex-matched controls with normal renal function were assayed and compared.

Serum creatinine, urea, inorganic phosphate and alkaline phosphatase were measured by standard techniques. Creatinine clearance was calculated using Schwartz formula $[0.55 \times \text{height (cm)} \div \text{serum creatinine (mg/dL)}]$.

All statistical analysis and significance of difference between groups were determined by unpaired Student's 't' test. Correlation coefficients were calculated using Pearson correlation.

Results

CRF cases were divided into four groups based on their creatinine clearance values(8,9): (a) mild CRF, clearance 50-75 mL/min/1.73 m² (n = 6), (b) moderate CRF, clearance 25-50 mL/min/1.73 m² (n = 7), (c) severe CRF, clearance 10-25 mL/min/1.73 m² (n = 15), and (d) ESRD, clearance 10 mL/min/1.73 m² (n = 16).

The mean age of different groups of study subjects were 9.17 ± 3.98, 6.32 ± 3.59, 8.60 ± 4.74, 9.75 ± 2.95 and 7.45 ± 3.59 years in mild, moderate, severe, ESRD and control, respectively. Out of 44 CRF cases, 30 (68.2%) were males and 14 (32.8%) females, with a male-female ratio of 2.14:1, and in control 12 (60%) were males and 8 (40%) females, with a male-female ratio of 1.5 : 1.

Mean creatinine clearance, iPTH, calcium, inorganic phosphate and alkaline phosphatase values of different groups are listed in *Table I*. Mean serum iPTH level was significantly elevated in mild CRF (P <0.05) than in the control group. In ESRD group, elevation of mean iPTH value was highly significant compared to all other groups (P <0.001). Even in severe CRF, elevation of mean iPTH value was significant than in comparison with mild group (P <0.05). Level of mean serum calcium was significantly lower in mild CRF (P <0.001) than in control group. In severe CRF group, mean serum calcium level was significantly lower than both mild and moderate CRF groups (P <0.05). The mean serum calcium in ESRD group had significant lower level compared to all other groups (P <0.001). Correction formula of serum

calcium with serum albumin level was not used in this study. Mean level of serum inorganic phosphate in mild CRF was significantly higher compared to control group (P <0.01). Mean serum inorganic phosphate in ESRD group was significantly higher compared to mild (P <0.001), moderate (P <0.01) and severe (P <0.05) groups. Mean serum inorganic phosphate in severe group was also significantly higher (P <0.01) compared to both mild and moderate CRF groups. Mean serum alkaline phosphatase was significantly higher in mild CRF compared to control group (P <0.01). In ESRD group, mean serum alkaline phosphatase was significantly higher than all other groups (P <0.001).

Serum iPTH negatively correlated with creatinine clearance (r = -0.564, P <0.001) and serum calcium (r = -0.507, P <0.001). Serum iPTH level positively correlated with inorganic phosphate (r = +0.345, P < 0.05) and serum alkaline phosphatase (r = +0.469, P <0.001).

Discussion

Present study was undertaken to assess iPTH in children with CRF and to correlate the levels with other biochemical parameters. In the present study it was observed that plasma concentration of mean iPTH was significantly increased in mild renal failure as compared to age-matched controls with normal kidney function. All the patients of moderate renal failure had increased level of iPTH and none of them had iPTH within normal range (7-53 pg/mL). The iPTH levels in mild CRF were within normal limit in all but one patient, but their mean level was 48.50 ± 4.76 pg/mL, which is nearer to upper limit of the normal range. The level of serum iPTH was higher in more advanced renal failure, thus confirming the relationship between

TABLE I—Mean Values of Creatinine Clearance and Biochemical Parameters in Control and CRF Groups.

Groups	CCR (mL/ Min/1.73 M ²)	iPTH (pg/mL)	Calcium (mg/dL)	Inorganic phosphate	Alkaline phosphatase (U/L)
Control (n = 20)	95.95 ±13.30	16.52 ±9.35	9.50 ±0.64	3.95 ±0.48	125.60 ±35.58
Mild (n = 6)	59.17 ±8.52	48.50 ±4.76	8.28 ±0.35	4.63 ±0.39	191.83 ±58.36
Moderate (n = 7)	34.98 ±7.75	67.29 ±7.91	8.10 ±1.00	4.96 ±0.65	250.57 ±101.43
Severe (n = 15)	17.71 ±5.40	82.42 ±9.67	7.41 ±0.75	5.79 ±0.83	291.67 ±120.67
ESRD (n = 16)	6.46 ±1.71	130.86 ±58.74	6.49 ±0.77	6.52 ±1.09	521.63 ±173.99
Total CRF (n = 44)	22.02 ±18.53	93.00 ±46.92	7.30 ±1.02	5.76 ±1.11	355.14 ±85.53
P values					
Control vs mild	<0.001	<0.05	<0.001	<0.01	<0.01
Mild vs moderate	<0.001	NS	NS	NS	NS
Mild vs severe	<0.001	<0.05	<0.05	<0.01	NS
Mild vs ESRD	<0.001	<0.001	<0.001	<0.001	<0.001
Moderate vs severe	<0.001	NS	<0.05	<0.01	NS
Moderate vs ESRD	<0.001	<0.001	<0.001	<0.01	<0.001
Severe vs ESRD	<0.001	<0.001	<0.001	<0.05	<0.001

severity of hyper-parathyroidism and the degree of renal impairment.

It was originally proposed that hypocalcemia triggers hyperparathyroidism in early renal failure(10). In our study, increased levels of mean serum iPTH were present even in early renal failure, and it was related to low mean serum calcium level and progressive rise of serum inorganic phosphate from early to advanced renal failure. Other authors have observed that serum total calcium concentration was normal in mild renal failure(11).

In the present study, significant levels of hypocalcemia and hyperphosphatemia were

present in advanced renal failure, such as severe CRF and ESRD. Other authors also observed that significant hyperphosphatemia usually occurs only in advanced renal failure, when GFR declines to 30 mL/min/1.73 m² rather than in early renal failure(12,13).

In our study, the mean values of serum alkaline phosphatase levels were within normal range in all but ESRD group. In the present study, though in all groups the mean values were within normal range, but values had a tendency of progressive rise from early to advanced renal failure. This finding is significantly related with secondary hyperparathyroidism in CRF.

Key Message

- Increased iPTH level is observed even in early renal failure, due to progressive hypocalcemia and hyperphosphatemia.

In conclusion, serum iPTH level were high even in early renal failure, and higher values directly related to the degree of renal failure. Progressive hypocalcemia and hyperphosphatemia are the initiating factors for the development of hyperparathyroidism.

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