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Status of Parathyroid Hormone in Maintenance Hemodialysis Patients

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Abstract **Original Research Article**

***Background**:* Numerous negative outcomes of Chronic Kidney Disease (CKD) receiving maintenance haemodialysis (MHD) are linked to secondary hyperparathyroidism (SPTH), hypocalcaemia and hyperphosphataemia. Its management is difficult for these patients. Currently, appropriate haemodialysis (HD) is maintained, and parathyroid hormone (PTH) is reduced with vitamin D receptor analogs (VDRA) and/or calcimimetics or parathyroidectomy. **Objective** :The main objective of this study was to evaluate the status of parathyroid hormone in maintenance Hemodialysis patients in Bangladesh. ***Method**:* This observational study was conducted in the haemodialysis unit of National Institute of Kidney Disease and Urology (NIKDU) and Bangladesh Institute of Research & Rehabilitation on Diabetes, Endocrine and Metabolism (BIRDEM). Patients getting maintenance haemodialysis in NIKDU and BIRDEM were enrolled in this study. ***Results**:* The mean age of the patients was 50.4±13.13 years. Male female ratio was 1.3:1. The mean BMI was 23.5±4.7 kg/m2 with range from 15.6 to 45.5 kg/m2. 114(95.0%) patients had HTN and 56(46.7%) patients had DM. The duration of haemodialysis was 25.55±25.0 months and 71 (59.2%) patients had twice haemodialysis session/weeks. Mean duration on hemodialysis was 23 ± 19 months (Range 2-124). ***Conclusion**:* The majority of our hemodialysis patients weren't dialyzed properly.

Keywords: Parathyroid hormone, Hemodialysis, Chronic kidney disease, Parathyroidectomy, vitamin D receptor analogs.

INTRODUCTION

Chronic kidney disease has become a major health concern with a high prevalence worldwide. An estimated 150 million people in Asia, or one in ten, are thought to have some form of kidney impairment. Hemodialysis (HD) patients experience deficits in trace elements [1].

Mineral and bone metabolism disorders are prevalent in CKD patients [2-4] and may contribute to the remarkably high death rates observed in these patients [5-7]. A wide range of pathologic conditions are included in these disorders, such as the conventionally recognized secondary hyperparathyroidism (SHPT), which is linked to elevated levels of parathyroid hormone (PTH) in the blood [8], as well as calcium and phosphorus imbalances, problems with vitamin D metabolism, renal osteodystrophy, and various forms of vascular calcification [9]. We now treat patients with CKD on a daily basis since certain anomalies that define the condition's mineral and bone problem seem amenable to therapeutic approaches. One of them is SHPT, which is thought to be caused, at least in part, by the increasing decrease in activated vitamin D levels with progressing CKD stages [10]. Thus, the primary method for treating SHPT is pharmacologic replacement therapy with vitamin D receptor activators (VDRA) [11]. This seemingly counterintuitive observation, which defies the dosage-response phenomenon expected in causal associations [12], may be caused by confounding by medical indication, as patients with more severe hyperparathyroidism (which is associated with higher serum PTH levels) may be given higher dosages of VDRA [16], despite the fact that these patients typically

have worse survival and defy the dosage-response phenomenon expected in causal associations [12].

OBJECTIVE

The main objective of this study was to uate theeval status of parathyroid hormone in maintenance Hemodialysis patients in Bangladesh.

METHODOLOGY

This cross-sectional study was conducted in the haemodialysis unit of National Institute of Kidney Disease and Urology (NIKDU) and Bangladesh Institute of Research & Rehabilitation on Diabetes, Endocrine and Metabolism (BIRDEM). The patients getting maintenance haemodialysis in National Institute of Kidney Disease and Urology (NIKDU) and Bangladesh Institute of Research & Rehabilitation on Diabetes, Endocrine and Metabolism (BIRDEM) were enrolled in this study. Blood specimens were collected with needling from the Arterio- Venos Fistula (AVF) for measurement of serum creatinine, serum albumin, calcium, iPTH. Specimens were allowed to clot at room temperature. Serum was separated from the cells by centrifugation. Serum creatinine, serum calcium, serum albumin, serum iPTH was measured by automated analyzer, Humalyzer 3000, Germany. Serum iPTH was quantitatively measured by IMMULITE 2000, is a solid phase, two site chemiluminescent enzyme-leveled immunometric assay in Department of Microbiology of Bangabandhu Shiekh Mujib Medical University (BSSMU). Calcium was corrected by using Payne's formula. Data were collected from both primary and secondary sources. Secondary data were collected from different published journal articles and research data base like Pubmed, Scopus and other reliable sources. The results of this study formulated with the combination of primary and secondary data and the sources of data was acknowledged by the author.

Collected data were compiled and appropriate analyses were done by using computer-based software, Statistical Package for Social Sciences (SPSS) version 23. Results were expressed as frequency, percentage and mean±SD.

RESULTS

Table 1 shows that mean age of the patients was 50.4±13.13 years. Male patients were predominant in this study. Male female ratio was 1.3:1. BMI of the study patients, it was observed the mean BMI was 23.5±4.7 kg/m2 with range from 15.6 to 45.5 kg/m2. 114(95.0%) patients had HTN and 56(46.7%) patients had DM.

Table 1: Distribution of age and gender of the study population

Patients Profile	Number of Patients	Percentage
Age (Years)		
Mean±SD	50.4±13.31	
Range (min-max)	(19-76)	
Sex		
Male	67	55.8
Female	53	44.2
BMI (kg/m2)	23.5±4.7	
Range (min-max)	(15.6-45.5)	
HTN	114	95
DM	56	46.7

Table 2 shows that duration of haemodialysis was 25.55±25.0 months and 71 (59.2%) patients had twice haemodialysis session/weeks. See the table below-

Table 2: Distribution of the study patients related to haemodialysis (n=120)

Haemodialysis (months)	Number of patients	Percentage
<6	8	6.7
6-18	52	43.3
>18	60	50.0
Mean±SD	25.55±25	
Range (min- max)	(1.5-228)	
Haemodialsysis session/Wk		
Twice(<8 hours)	71	59.2
Thrice(>8 hours)	49	40.8

Achievement of the four recommendations of K/DOQI guidelines was only 9(7.5%). See the Figure 1 below-

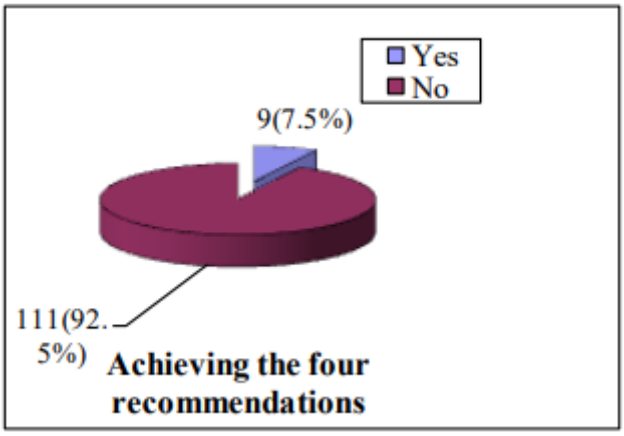

Figure 1: Showing achievement of the four recommendations of the study patients

Table 3 shows baseline demographic, clinical, and laboratory characteristics of the studied MHD patients, who received paricalcitol in any one of the three paricalcitol index groups. See the table 1 below-

Table 3: Baseline data of MHD patients

Parameter Serum (mean ± SD)	Paricalcitol-to-PTH Ratio (g/wk per pg/ml)		
	1 to 30	30 to 60	≥60
creatinine (mg/dl)	8.90 ± 3.16	8.90 ±5.20	8.57± 3.10
albumin (g/dl)	2.94± 0.27	4.73 ± 0.34	4.35± 0.37
calcium (mg/dl)	8.80 ± 0.70	9.34± 0.70	7.50 ± 0.70
phosphorus (mg/dl)	7.10 ± 1.40	6.34± 1.40	6.60 ± 1.30
iPTH (pg/ml)	548.00 ± 395.00	362.00 ± 459.00	194.00 ± 134.00

iPTH, intact parathyroid hormone; MHD, maintenance hemodialysis; TIBC, total iron-binding capacity

Table 4 shows the duration on hemodialysis in months of study population. Mean duration on hemodialysis was 23 ± 19 months (Range 2-124). Most patients were on hemodialysis below 12 months. See the table below-

Table 4: Duration on hemodialysis in months of study population

Duration on hemodialysis	Frequency	Percent
2-6	20	16.7
7-12	28	23.3
13-18	16	13.3
19-24	17	14.2
25-30	6	5.0
31-36	10	8.3
37-42	2	1.7
43-48	9	7.5
>48	12	10.0

According to previous study intradialytic complications were hypertension 14 (5.8%), hypotension 10 (4.1%), shivering 9 (3.7%), sweating 7 (2.9%), leg cramp 5 (2%), Headache (1.2%) [13].

DISCUSSION

In terms of morbidity and mortality in chronic hemodialysis patients, adequate dialysis is a crucial factor [14]. The basic goals of dialysis therapy are to increase quality of life, decrease morbidity, and extend patient longevity. But despite numerous technological developments over the past few years, dialysis patients' morbidity and mortality rates continue to be very high, and their quality of life is frequently poor. The morbidity and mortality of dialysis patients might be impacted by the dialysis dose that is administered. Additionally, during the past ten years, a number of epidemiological studies, primarily based on longitudinal database registries, have raised the possibility that convective dialysis treatments are preferable in terms of enhancing patient outcomes. As a result, in addition to the administered dose of dialysis, the size of molecules eliminated can also be crucial [15]. The high death rate in ESRD patients can be attributed to inadequate dialysis. Hemodialysis is often done twice a week due to a variety of reasons, including logistical and

economical constraints [16]. The elimination of nitrogenous solutes is typically understood to be the goal of adequate dialysis. Measures of urea removal are frequently used as stand-ins for nitrogenous solute removal, despite the fact that urea is non-toxic and only represents tiny solutes. The Urea Reduction Ratio (URR) and the mathematically related Kt/V urea are the urea elimination measurements that are most frequently utilized in clinical practice [16].

Better survival was associated with higher levels of the paricalcitol dosage to serum PTH concentration ratio. This correlation was found in analyses utilizing limited cubic splines as well as categorical analyses based on four groups of paricalcitol to PTH ratio that were predetermined. The mainstay of treatment for SHPT in the CKD patient population has been vigorous vitamin D replacement [12]. Early on in the progression of CKD, SHPT appears as a result of a confluence of factors that includes calcitriol shortage, reduced expression of the calcium-sensing receptor and the vitamin D receptor, hyperphosphatemia, hypocalcemia, and PTH resistance [12]. PTH levels rise steadily as renal function decreases in CKD patients, which is paralleled by a steady reduction in activated vitamin D levels [4]. Thus, replacing physiologic amounts of this hormone with synthetic activated vitamin D administration appears to be a viable treatment option for SHPT. However, physiologic doses of activated vitamin D frequently fail to treat SHPT, in part due to reduced parathyroid gland expression of the vitamin D receptor [17]. Higher doses of activated vitamin D may be given to circumvent this, but these pharmacologic doses are more likely to cause side effects. Hypercalcemia and hyperphosphatemia [18], which have already been linked to greater mortality in patients on dialysis [4], are the most pertinent of these adverse effects.

In order to avoid these negative consequences, new medicines that decrease PTH generation more selectively while having less of an impact on calcium and phosphorus absorption in the intestine and the bones have been created. These brand-new activated vitamin D analogs appear to have less of an impact on the bone and gastrointestinal vitamin D receptors, which reduces calcium and phosphorus absorption and expands the therapeutic window [12]. Despite these findings, there is still disagreement over the idea of VDRA selectivity and its use in clinical practice [8]. The advantages of VDRA may go beyond the conventional PTH-lowering impact and may have direct cardiovascular and metabolic effects, according to recent data from many sizable observational studies [19]. Therefore, a combination of the beneficial benefits, including but not limited to the drop in PTH level, may be to blame for the longer survival of CKD patients reported in connection with the VDRA. We proposed that confounding by indication caused earlier research to miss an advantageous benefit of increasing VDRA dosage [20].

In MHD patients with low PTH levels, the current recommendations advise reducing the dosage or even stopping VDRA due to concerns about the so-called "adynamic bone disease" [21]. A recent research of males who did not yet receive dialysis and had mild to severe CKD discovered a strictly rising relationship between serum PTH and survival [22]. Numerous cardiovascular, metabolic, hematologic, and immunologic problems, such as decreased cardiac contractility, myocardial calcium deposition, vascular calcification, and aberrant immunological function, have been linked to elevated PTH levels [22]. If the PTH-survival relationship is causative, it might explain why vitamin D analogs that reduce PTH levels are linked to better survival. It is significant to note that the group with the greatest paricalcitol-to-PTH ratio also had higher serum calcium levels. It is therefore probable that high calcium levels caused a relative suppression of PTH and an increase in ratio [5]; however, hypercalcemia is typically linked to an increased mortality in MHD patients, whereas individuals in the study's latter group had the highest survival rates.

CONCLUSION

The majority of our hemodialysis patients weren't dialyzed properly. Different study showed that intradialytic complications like hypertension, hypotension, shivering, sweating, leg cramp, and headache observed in some cases among the patients. Multicenter and wide range study required for the proper management of these patients.

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