The Prevalence and Outcome of Parathyroid Disorder After Renal Transplantation: A Prospective Observational Study

Dear Editor,

There is a well-recognized association between chronic kidney disease (CKD) and mineral bone disease. Renal transplantation restores calcium, phosphorous, and vitamin D levels leading to decline in levels of serum parathyroid hormone (PTH). The prevalence of parathyroid disorder in post-transplant recipients is variable.[1-4] There are few Indian data regarding the prevalence of parathyroid disorder in kidney transplant recipients. This prospective, observational study aimed to assess the prevalence of parathyroid disorder in renal transplant recipients during 12 months of transplantation and identify the association of parathyroid disorder with demographics/clinical variables. The study protocol was approved by institutional ethics committee.

Demographic characteristics of 52 post-transplant recipients are shown in Supplementary Table 1. Of 52 patients, two were lost to follow-up and one expired after 3 months, and one patient expired after 6 months of transplantation. Analysis was done considering 52, 49, and 48 patients, respectively at 3, 6, and 12 months after transplantation.

At baseline serum iPTH <65 and ≥65 pg/ml were found in 8 (15.38%) and 44 (84.61%) patients, respectively. At 3-month, 43 (82.7%) had hyperparathyroidism, and 9 (17.30%) had normal PTH levels. At 6-month, 45 (91.8%) had hyperparathyroidism, and 4 (8.2%) had normal PTH levels. At 12-month, 38 (79.2%) had hyperparathyroidism, and 10 (20.8%) had normal PTH levels. Pre-transplantation mean iPTH levels were 370.496 ± 419.26 pg/ml, and post-transplantation, these values were 237.496 ± 244.13 pg/ml, 184.420 ± 165.59 pg/ml, and 205.975 ± 250.09 pg/ml, at 3, 6, and 12 months, respectively. Table 1 outlines the levels of biochemical parameters at baseline and post-transplantation. Supplementary Figure 1 shows the trend of changes in glomerular filtration rate (eGFR), serum PTH, calcium, phosphorus, and vitamin D post-transplantation. Table 2 presents the association of post-transplant hyperparathyroidism months with demography/clinical variables. Supplementary Figure 2 depicts scatter plots for all significant associations. The mean iPTH levels were significantly higher in patients with eGFR <60 ml/min/1.73 m^2 than ≥60 ml/min/1.73 m^2 (310.694 pg/ml vs. 143.143 pg/ml, $P = 0.023$). More details are available in Supplementary Materials and Methods.

The pre-transplantation mean serum iPTH levels, in our study, are comparable to values reported by Gomes *et al.*[5] (300 pg/ml) and Wolf *et al.*[6] (423.4 ± 340.1 pg/ml). The prevalence of hyperparathyroidism (defined as ≥65 pg/ml) was 82.7%, 91.8%, and 79.2%, respectively, at 3-, 6-, and 12-month post-transplantation, which are approachable to figures reported in two Indian studies. The first study published by Rathi *et al.*,[S7] showed the prevalence of 42.7% and 51.3%, respectively, at 12- and 24-week post-renal transplantation. Aggarwal *et al.*[S8] showed the high, normal, and low PTH levels (as per the Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines for the range of eGFR) in 69%, 22%, and 9% of cases. Our patients had achieved normal post-transplantation serum calcium and phosphorus levels. At 12-month, the incidence of hypercalcemia was less (4.17%) than observed in studies published by Gomes *et al.*[5] (24%) and Torres *et al.*[S9] (75%). High prevalence of vitamin D deficiency is most likely attributable to less events of hypercalcemia in our population.

Post-transplant PTH levels (at 3-, 6-, and 12-month) correlated with pre-transplant PTH levels. Disease duration and dialysis vintage showed a significant effect in the early post-transplantation period at 3-month, which was not observed on further follow-up. This could be explained by that pre-transplant factors (i.e. duration of disease) may be decisive in early post-transplantation period; however, as time progresses, post-transplant factors (i.e. eGFR) play a crucial role in severity of hyperparathyroidism. GFR is generally considered as the best index for graft function.[S10] Our cohort achieved relatively good graft functions with mean estimated GFR of 79.44 ml/min/1.73 m^2, 72.80 ml/min/m^2, and 71.29 ml/min/m^2 at 3-, 6-, and 12-month post-transplantation. Comparatively, Bleskestad *et al.*[S11] and Gomes *et al.*[5] reported the mean eGFR of 70.9 ml/min/m^2 and 58.1 ± 18.7 ml/min/mm^2, respectively, at 1-year post-transplantation. Recent Indian study by Aggarwal *et al.*[S8] stated almost patients achieved eGFR >60 ml/min/m^2. Post-renal transplant recipients had eGFR ≈ 30–60 mL/min/1.73 m^2, hinting some degree of reduced kidney function resulting in CKD-related hyperparathyroidism.[S12] We discovered that hyperparathyroidism was not correlated with serum creatinine and eGFR at 3- and 6-month, but it was correlated at 12-month. These findings suggest the role of post-transplant factors (i.e. serum creatinine and eGFR) as a long-term predictor for hyperparathyroidism; however, further studies are warranted to validate this claim.

Our study was limited by small sample size and short follow-up. Further, the fibroblast growth factor (FGF) 23 levels and bone mineral density were not assessed. In conclusion, hyperparathyroidism continued up to 12-month post-transplantation. Vitamin D deficiency/

Table 1: Levels of various biochemical parameters (pre-transplantation and after 3, 6, and 12 months of transplantation)

Biochemical parameter	Baseline (*n* = 52)	3-month follow-up (*n* = 52)	6-month follow-up (*n* = 49)	12-month follow-up (*n* = 48)
Mean iPTH levels (range), pg/ml	370.50 ± 419.26	237.50 ± 244.13	184.42 ± 165.59	205.975 ± 250.09
iPTH levels, *n* (%)	(2.5-2267)	40.2-1294)	(32.6-840)	(31.5-1295)
<65 pg/ml	8 (15.38)	9 (17.31)	4 (8.16)	10 (20.83)
≥65 pg/ml	44 (84.61)	43 (82.69)	45 (91.84)	38 (79.17)
Mean sr. creatinine (range), mg/dl	-	1.2608 ± 0.62	1.3527 ± 0.68	1.3035 ± 0.50
		(0.30-4.8)	(0.40-50)	(0.5-3.60)
Mean GFR (range), ml/min/1.73 m^2	-			
MDRD formula		79.44 ± 65.23	72.8094 ± 47.41	71.2919 ± 37.14
		(15.20-489)	(14.50-342)	(21.10-264)
Nankivell formula		73.0579 ± 26.47	68.82 ± 24.12	67.5583 ± 21.52
		(7.00-194)	(7.02-149)	(15.20-119)
Mean sr. calcium (range), mg/dl	-	9.2490 ± 0.45	9.3555 ± 0.41	9.2885 ± 0.5
Sr. calcium levels, *n* (%)		(8.20-10.20)	(8.50-10.50)	(8.3-10.40)
Hypocalcemic (<8.6 mg/dl)	21 (40.38)	4 (7.7)	1 (2.04)	4 (8.33)
Hypercalcemic (8.6-10.2 mg/dl)	1 (1.9)	-	47 (95.91)	2 (4.16)
Normocalcemic (>10.2 mg/dl)	30 (57.69)	48 (92.30)	1 (2.04)	42 (87.5)
Mean sr. phosphorus levels (range), mg/dl	-	3.704 ± 0.71	3.596 ± 0.66	3.679 ± 0.68
Sr. phosphorus levels, *n* (%)		(2.2-5.4)	(2.5-5.6)	(2.7-6.2)
Hypophosphatemia <2.5 mg/dl	3 (5.76)	2 (3.84)		
Hyperphosphatemia >4.5 mg/dl	32 (61.53)	6 (11.53)	9.3555 ± 0.41	7 (14.58)
Normophosphatemic 2.4-4.5 mg/dl	17 (32.69)	44 (84.61)	(8.50-10.50)	41 (85.41)
Mean sr. total vitamin D levels	-	12.0535 ± 6.09	7 (14.28)	19.4915 ± 9.24
		(3.0-25.0)		(4.0-48.20)
Vitamin D deficiency <20 ng/ml		47 (90.38)	42 (85.71)	33 (68.75)
Vitamin D insufficiency 21-29 ng/ml		5 (9.61)	16.1018 ± 10.45	9 (18.75)
Normal >30 ng/ml		-	(4.0-67.90)	6 (12.5)

Sr.: Serum; GFR: Glomerular filtration rate; MDRD: Modification of Diet in Renal Disease Study. Out of the total 52 patients, two were lost to follow-up (i.e., one patient expired post 3-month of transplantation and one post 6-month of transplantation); therefore, statistical analysis was carried out on 52, 49, and 48 patients, respectively, at 3-, 6-, and 12-month post-transplantation

Table 2: Correlation of post-transplantation hyperparathyroidism with multiple factors

Correlation of post-transplantation hyperparathyroidism with	*P*		
	3-month follow-up		
	(*n* = 52)	(*n* = 49)	(*n* = 48)
Age	0.298	0.254	0.422
Sex	0.134	0.943	0.471
Pre-transplantation hyperparathyroidism	0.001**	0.001**	0.001**
Duration of disease	0.030*	0.074	0.161
Dialysis vintage	0.060	0.031*	0.044*
Serum creatinine	0.477	0.197	0.006*
eGFR (MDRD as well as Nankivell equation)	0.432	0.219	0.030*

**$P \leq 0.001$ and *$P < 0.05$ considered as significant, eGFR: estimated glomerular filtration rate; MDRD: modification of diet in renal disease.

insufficiency was common in post-transplant recipients. Pre-transplantation factors affected the parathyroid status in the early post-transplantation period, while post-transplantation factors impacted the parathyroid status in the late post-transplant period.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Conflicts of interest

There are no conflicts of interest.

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Ambulatory Hypertension in Children with Kidney Failure on Maintenance Dialysis

Dear Editor,

Cardiovascular (CV) disease is the leading cause of death in children with advanced chronic kidney disease (CKD).[1] Indian children with CKD have a higher prevalence of CV morbidity compared to the Western pediatric CKD cohort.[2] Limited data are available on the prevalence of hypertension (HTN) in children with kidney failure on maintenance dialysis.

Traditionally, blood pressure (BP) in children on dialysis is measured manually in the clinic, which may be inaccurate due to fluctuations in fluid status and diurnal variations.[3] Ambulatory BP monitoring (ABPM) has the advantage of detecting diurnal variations in BP over a 24-h period. The objectives of this study were to determine the prevalence of uncontrolled HTN by ABPM versus clinic BP measurement alone in children with kidney failure on maintenance dialysis, to assess the diurnal variation of ambulatory BP and to determine factors associated with ambulatory HTN. For detailed description of methods refer to the Supplementary Material.

Twenty-seven patients (12 ± 2.6 years) consisting of 13 (48%) girls, with 18 (67%) on peritoneal dialysis (PD), having a median dialysis vintage of 17 months (10–35 months) were included. Residual kidney function was present in 16 patients (59%). Concentric left ventricular hypertrophy (LVH) was present in 19 (70%) patients. Twenty-six patients (96%) already had a diagnosis of HTN and were on treatment, with a median of three antihypertensive medications. The patient characteristics are described in Table 1.

Table 1: Clinical characteristics of children with kidney failure on maintenance dialysis

Characteristic	Value
Total patients	27
Girls	13 (48%)
Patients on PD	18 (67%)
Age (years)	12 (±2.6)
Dry wt z-score	−3.2 (±2.3)
Ht z-score	−3.18 (±1.9)
Non-glomerular native kidney disease	17 (63%)
Dialysis vintage (months)	17 (10-35)
IDWG (wt gain above the dry weight as a percentage of body weight)	2.5% (±2.16%)
Patients with LVH	19 (70%)
HTN by clinic BP alone	17 (63%)
HTN by ABPM	22 (81%)
Isolated nocturnal HTN, *n* (%)	4 (18%)
Blunted nocturnal dip, *n* (%)	24 (89%)

Data presented as *n* (%), mean (±SD), or median (IQR). ABPM = ambulatory blood pressure monitoring, DBP = diastolic blood pressure, HTN = hypertension, IDWG = intradialytic weight gain, LVH = left ventricular hypertrophy, PD = peritoneal dialysis, SBP = systolic blood pressure, wt: weight.

Despite the patients being on antihypertensive medication, ABPM identified uncontrolled HTN in 22 (85%) patients and one patient had a newly diagnosed HTN. In contrast, clinic BP monitoring detected uncontrolled HTN in only 17 patients (65%). Therefore, in five patients, HTN was diagnosed only by ABPM (four had masked uncontrolled HTN and one was newly diagnosed). The level of