POST RENAL TRANSPLANTATION HYPOPHOSPHATEMIA IS ASSOCIATED WITH HIGH FGF23 LEVEL

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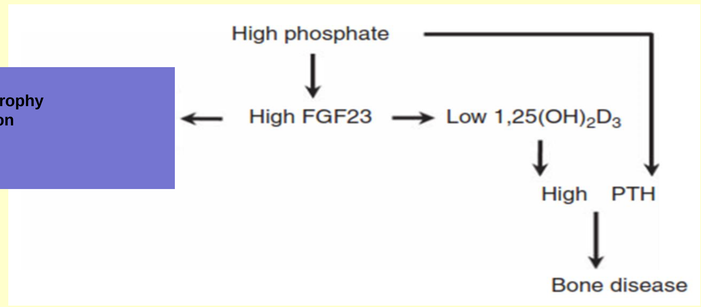
Introduction:

- Fibroblast growth factor 23 (FGF23) and iPTH are involved in calcium-phosphate homeostasis.
- Glomerular filtration of phosphorus is regulated by PTH and FGF23.

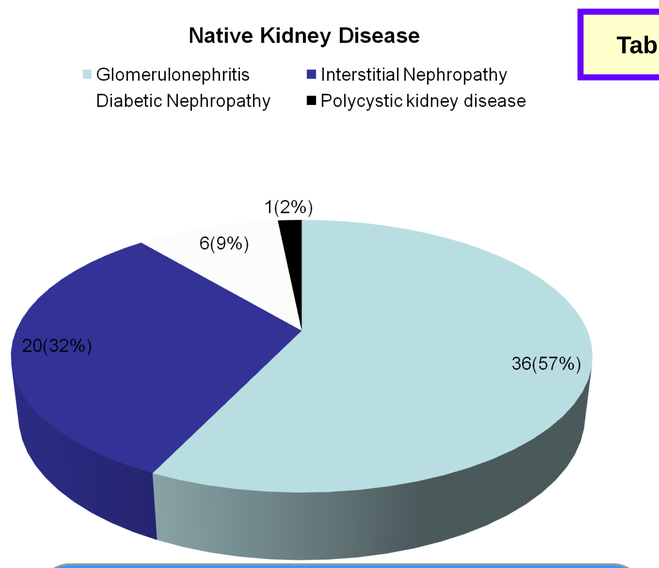


- Onset of hypophosphatemia in early post renal transplant period is of vital clinical significance.
- However, there is paucity of data on mechanism behind onset of hypophosphatemia in early post renal transplant period.
- Changes in FGF23, iPTH and other parameters in Indian scenario after transplantation.

Aim:

We aimed this study to determine the predictors of post renal transplant hypophosphatemia in living donor transplantation.

Material and Methods:



FGF23 analyzed by ELISA and iPTH, 25(OH) vitD, and other by Automated Analyzer

Table 1.Patients demographics and concomitant treatment

Characteristics	
Male/Female	58 /5
Mean Age (years)	35.65±11.79 (9-61)
Height (cm)	162.05±11.27
Weight (kg)	55±9.63
Body mass index (kg/m^2)	20.85±2.46
Dialysis duration (months)	9.83±7.58
Smoker (%)	7.9
Alcoholic (%)	6.3
Blood related Transplant	41 (65%)
Immune suppression agents (%)	
steroids	100
calcineurin inhibitor	
Tacrolimus	60 (95.2%)
Cyclosporine A	3 (4.8%)
mycophenolate mofetil	100
induction therapy	
Basiliximab	47 (74.6%)
ATG	6 (9.5%)
Phosphate binder (%)	
calcium based	45 (71.4%)
non-calcium based	18 (28.6%)

Statistical analysis

Data- mean±standard deviation
Wilcoxan test (two groups, non-normal distribution), **Independent sample T-test** (two groups, normal distribution)
Normality was assessed using the **Kolgomorov–Smirnov test**.
Correlations between different parameters **Pearson correlation**
Association between dependent and independent variables- **Linear regression analysis (backward stepwise)**
Analysis on **SPSS software ver. 17.0** (SPSS, Chicago, IL)

Results:

Table 2.Biochemical parameters

variable	Pre-Tx	Month 1
iPTH (pg/ml)	350.44±235.16*	112.3±84.38(↓67.95%)
Hyperparathyroidism (>65 pg/ml)	63(100%)	40 (63.5%)
FGF23 (pg/ml)	1367.4±807.24*	82.40±79.78(↓93.81%)
FGF23 (>50 pg/ml)	58(92%)	23(36.5%)
25(OH) Vit D (ng/ml)	27.29±12.35	23.54±9.56
eGFR (ml/min)	9.58±4.01	81.02±48.64
Inorganic phosphate (mg/dl)	6.42±2.12*	2.92±0.85
Hypophosphatemia (<2.5mg/dl)		17(27%)
creatinine (mg/dl)	7.49±1.93*	1.19±0.25
BUN (mg/dl)	53.54±22.51*	23.26±9.14
uric acid ()	6.76±1.99*	4.33±1.32
calcium (mg/dl)	8.62±0.82	9.24±0.50
Hypocalcemia (<8.5mg/dl)	26(41.3%)	
alkaline phosphatase (U/l)	182.02±97.75	99.86±50.27

Table 3 I Difference between Hypo and Normo-calcemic group

Before Tx	Hypocalcemia (n=26)	Normocalcemia (n=37)	P-value
iPTH	439.42±259.64	287.92±196.69	0.016
FGF23	1675.05±688.68	1151.22±882.5	0.008

Table 4 I Baseline clinical and laboratory data of 63 patients under going transplantation

Parameters	FGF23 (pg/ml) Tertile 1 ≤1054.50	Tertile 2 1054.51-1859.19	Tertile 3 ≥1859.20	P-value
iPTH (pg/ml)	220.28±119.60	318.72±123.74	512.33±308.95	0.001
25(OH) Vit D (ng/ml)	28.16±12.63	27.51±14.40	26.19±10.02	NS
eGFR (ml/min)	12.07±5.34	8.66±3.03	8.01±1.51	0.001
phosphate (mg/dl)	5.40±1.55	6.51±2.26	7.35±2.09	0.009
creatinine (mg/dl)	6.56±1.79	7.89±1.85	8.00±1.90	0.025
hemoglobin (gm/dl)	9.29±1.87	9.72±1.70	9.62±1.84	NS
BUN (mg/dl)	44.81±15.38	49.85±17.63	65.94±27.72	0.005
uric acid ()	5.91±2.14	6.96±1.64	7.40±1.95	0.042
calcium (mg/dl)	8.97±0.88	8.71±0.60	8.17±0.77	0.004

Table 5 I At pre-Tx, factors associated with serum iP (linear regression model constructed by backward stepwise modeling procedure) in models that features FGF23, iPTH or eGFR and iP.

Variables	Dependent variable: Pretransplant inorganic Phosphorous			
	Regression coefficient (B)	95% Confidence interval	P-value	r^2
Univariate linear regression				
iPTH	0.004	0.002 to 0.006	<0.001	24.2%
FGF23	0.001	0.001 to 0.002	<0.001	18.8%
eGFR	-0.156	-0.285 to -0.027	0.019	8.7%
BUN	0.037	0.015 to 0.060	0.001	15.8%
Uric acid	0.467	0.216 to 0.707	<0.001	18.8%
Non-veg			0.008	11.1%
Multivariate linear regression model (Backward method)				
iPTH	0.003	0.001 to 0.005	0.016	
FGF23	0.000	0.000 to 0.001	0.317	
Uric acid	0.252	0.008 to 0.496	0.043	
Non-veg			0.112	
Whole model			<0.001	
				41%

Table 6 I At M1, factors associated with serum iP (linear regression model constructed by backward modeling procedure) in models that features FGF23, iPTH or eGFR and iP.

Variables	Dependent variable: inorganic Phosphorous M1			
	Regression coefficient (B)	95% Confidence interval	P-value	r^2
Univariate linear regression				
FGF23(M1)	-0.006	-0.008 to -0.003	<0.001	28.8%
eGFR(M1)	0.004	0.000 to 0.009	0.052	6.1%
Uric acid(M1)	-0.174	-0.334 to -0.014	0.034	7.2%
Multivariate linear regression model (Backward method)				
iPTH(M1)	-0.001	-0.002 to -0.003	0.700	
FGF23(M1)	-0.005	-0.008 to -0.003	<0.001	
eGFR(M1)	0.003	0.000 to 0.007	0.082	
Uric acid(M1)	-0.051	-0.206 to 0.104	0.511	
Whole model			<0.001	
				33.1%

Conclusions:

✓After transplant levels of FGF23 normalize more rapidly than of iPTH.
✓Patients with higher pre-transplant inorganic Phosphorous level were more likely to develop hypophosphatemia after transplantation.
✓Role of FGF23 in iP homeostasis is more prominent to an early period after transplantation independent of PTH.

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