

# Biochemical parameters associated with serum intact FGF23 levels in patients with X-linked hypophosphatemic rickets

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## Background

Fibroblast growth factor 23 (FGF23) decreases renal phosphate reabsorption and serum 1,25-dihydroxyvitamin D [1,25(OH)<sub>2</sub>D] levels. X-linked hypophosphatemic rickets (XLH) is caused by mutations in the *PHEX* gene and accompanied by decreased serum inorganic phosphate (IP) and elevated serum FGF23 levels. Patients with XLH are generally treated with oral active vitamin D and phosphate, but some previous reports indicated that serum FGF23 levels increased with this treatment. However, biochemical parameters associated with serum FGF23 levels during the treatment in XLH patients remain unclear.

## Objective and hypotheses

To analyze parameters associated with serum intact FGF23 levels during treatment of XLH patients to obtain better outcomes

## Method

Subjects: 12 males and 4 females with XLH and normal kidney function

Follow-up duration: 5.6 ± 4.7 years

*PHEX* gene analysis: all exons were analyzed by Sanger sequencing in 11 patients of 8 families

Treatment: alphacalcidol (1αOHD) and phosphate (P) except for one patient treated with 1αOHD alone

Evaluated parameters: gender, age, height SDS, serum calcium (Ca), IP, creatinine (Cr), alkaline phosphatase (ALP), intact PTH (iPTH), intact FGF23 (Kainos) and 1,25(OH)<sub>2</sub>D levels and doses of 1αOHD and P

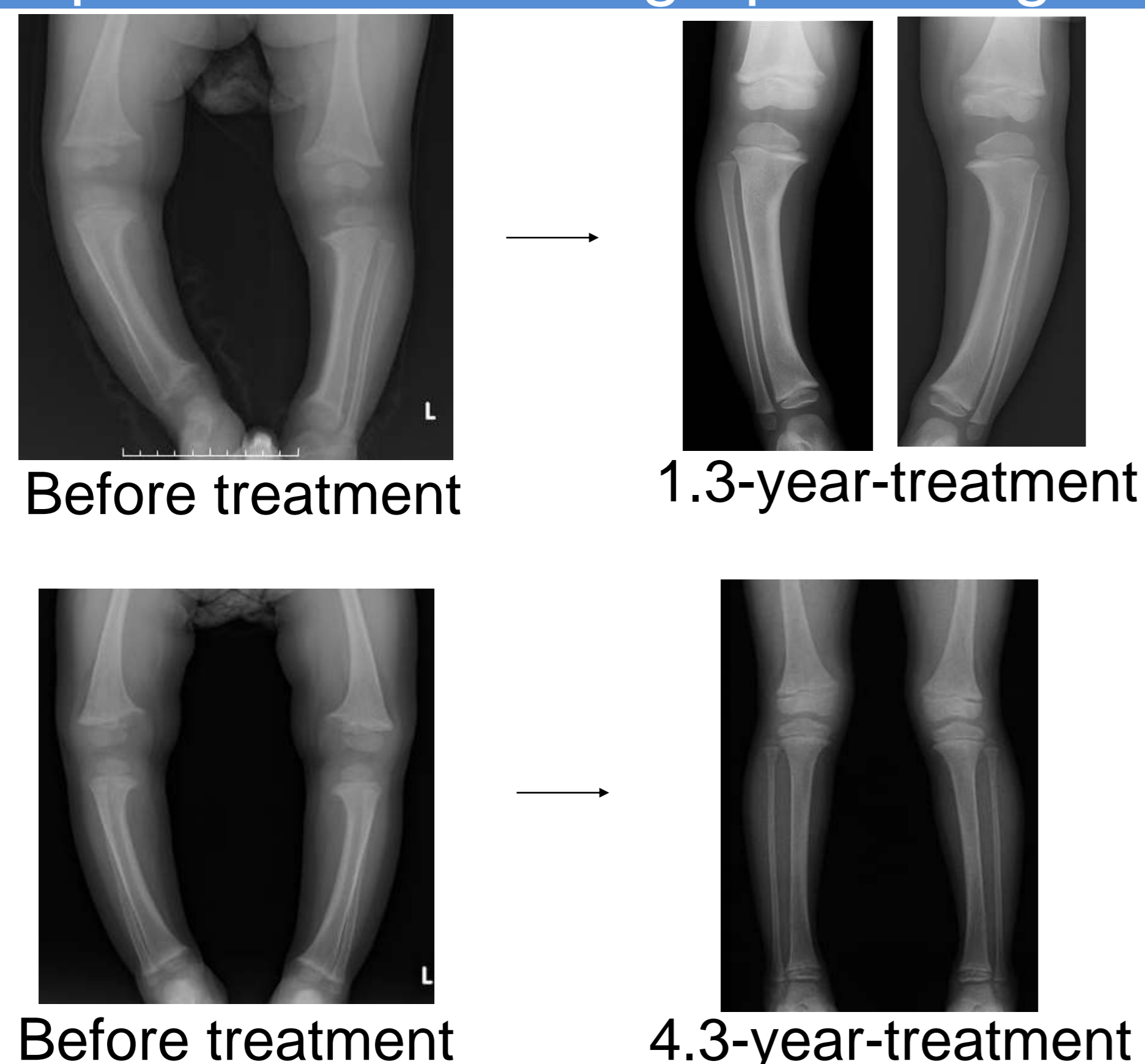
Statistic analysis: linear mixed-effects models in SPSS ver.23 software

## Results

### *PHEX* gene analysis

p.Pro534Leu	2 patients in 2 families
p.Gly579Arg	1 patient in 1 family
p.Gly648Arg	1 patient in 1 family
p.Arg702*	1 patient in 1 family
p.Arg747*	5 patients in 2 families
c.1769-1g>a	1 patient in 1 family

### Representative radiographic images



### Parameters at first and last visits

Visit	First	Last
Age (years)	2.48 ± 2.47	7.68 ± 5.69
Height SDS	-1.74 ± 0.85	-1.98 ± 1.06
Ca (mg/dl)	9.67 ± 0.51	9.34 ± 0.43
IP (mg/dl)	2.90 ± 0.49	3.04 ± 0.78
ALP (U/L)	1832 ± 676	1069 ± 470
iPTH (pg/ml)	61.4 ± 41.1	48.7 ± 25.3
1,25(OH) <sub>2</sub> D (pg/ml)	68.2 ± 28.0	71.8 ± 41.5
Cr (mg/dl)	0.23 ± 0.08	0.37 ± 0.16
<b>FGF23 (pg/ml)</b>	<b>73.4 ± 13.4</b>	<b>214.6 ± 248.7</b>
Dose of 1αOHD (μg/kg/day)	-	0.07 ± 0.05
Dose of P (mg/kg/day)	-	47.2 ± 35.2

Mean ± SD.

### Association of serum FGF23 levels with other parameters

	mean		difference	
	B	p	B	p
<b>Gender (female)</b>	470.23	<b>0.015</b>	-	-
<b>Age</b>	-57.34	0.167	-55.18	<b>0.000</b>
<b>Ca</b>	-189.36	0.358	217.93	<b>0.000</b>
<b>IP</b>	-352.74	0.226	89.97	<b>0.000</b>
<b>ALP</b>	-0.29	0.180	-0.080	<b>0.007</b>
iPTH	-7.20	0.169	-0.80	0.302
<b>1,25(OH)<sub>2</sub>D</b>	4.16	0.284	1.72	<b>0.001</b>
<b>Cr</b>	151.27	0.894	2241.55	<b>0.000</b>
Dose of 1αOHD	-703.23	0.478	-309.54	0.569
<b>Dose of P</b>	16.29	<b>0.002</b>	1.40	0.391

## Summary

Serum FGF23 levels were positively associated with serum Ca, IP, 1,25(OH)<sub>2</sub>D and Cr levels, female and the dose of P and negatively with age and ALP levels.

## Discussion

- These results indicate that serum Ca, IP and 1,25(OH)<sub>2</sub>D levels and the dose of P might be involved in FGF23 production in XLH patients.
- We might be careful not to overcorrect serum Ca, IP and 1,25(OH)<sub>2</sub>D levels during the treatment because increased FGF23 could exacerbate bone phenotypes and biochemical parameters.
- Considering the association with FGF23, gender, age and serum Cr levels could be involved in serum FGF23 levels in XLH patients, although their mechanisms are unclear.

## Conclusion

Serum FGF23 levels might be influenced by serum Ca, IP, and 1,25(OH)<sub>2</sub>D levels and the dose of P during the treatment of XLH patients

## Conflict of interest

Nothing to disclose

