Acquired FGF23 Resistance: The Primacy of Parathyroid Hormone over Fibroblast Growth Factor 23 in Renal Phosphorus Handling

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OBJECTIVES

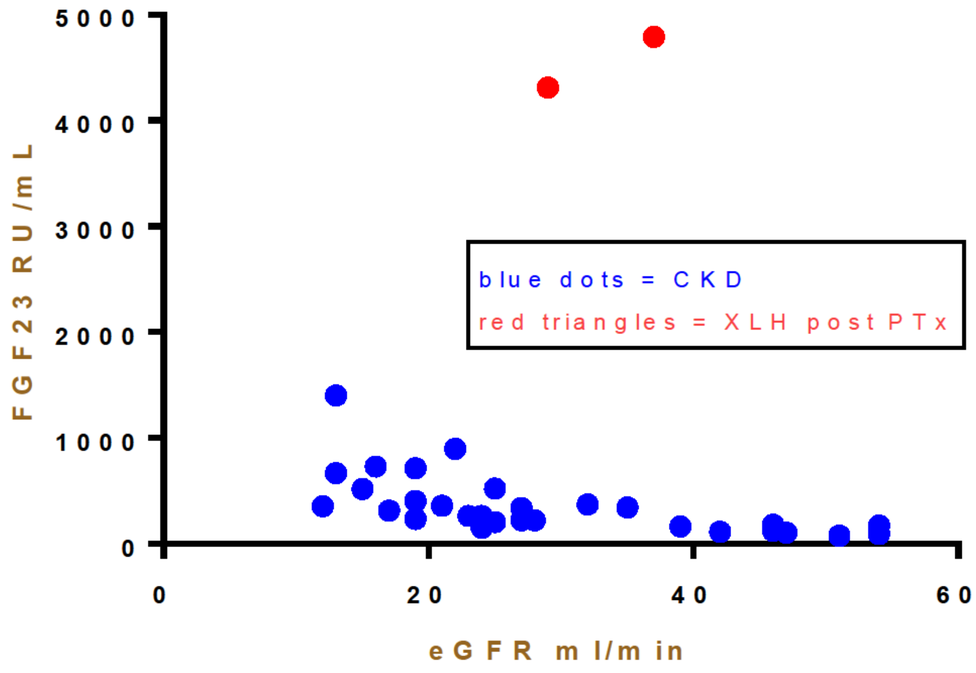
- Fibroblast growth factor 23 (FGF23) excess is the cause of chronic hypophosphatemia in rare conditions such as X-linked hypophosphatemic rickets (XLHR) and tumour-induced osteomalacia (TIO), but animal studies indicate that the effect of FGF23 on serum phosphorus is dependent on the presence of parathyroid hormone (PTH).
- In this case series of rare disorders with abnormalities in renal phosphorus handling, we sought to explore the relative roles of PTH and FGF23 on renal handling of phosphorus.

METHODS

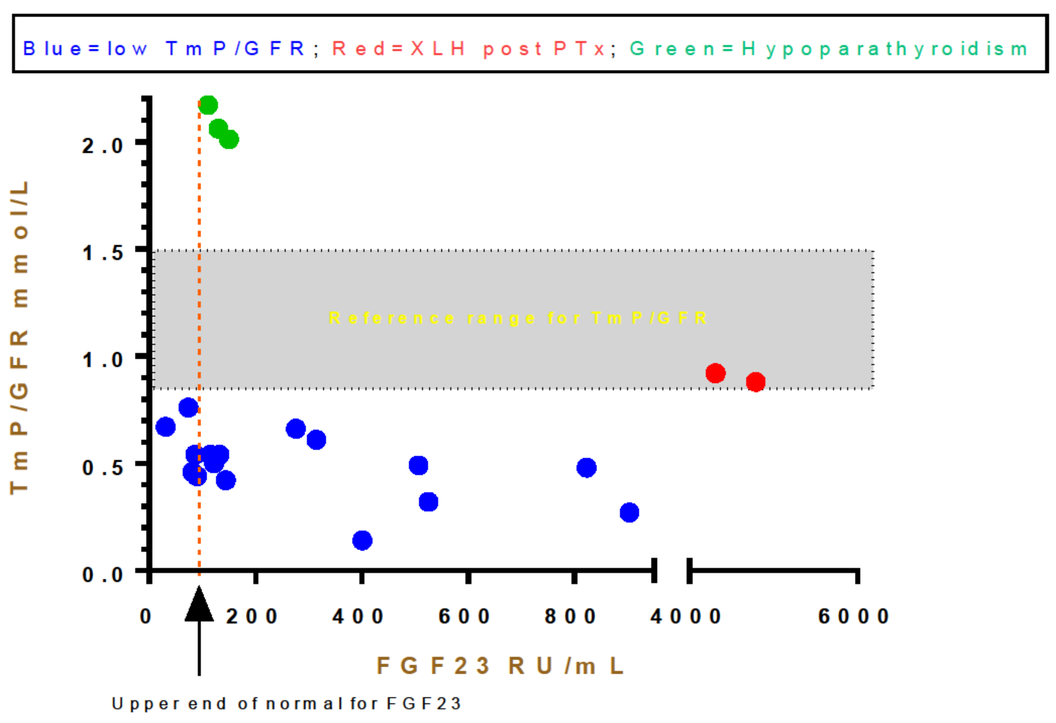
Study groups:
1.Congenital hypophosphatemia (n=14) and with hypoparathyroidism post parathyroidectomy (n=2)
2.TIO (n=2)
3.Renal tubular acidosis with phosphate-wasting and osteomalacia (n=1)
4.Hypoparathyroidism
5.Chronic kidney disease (n=30).
Analysis
1.Genetic mutation analysis,
2.Measurement of FGF23, PTH, renal phosphorus threshold (TmP/GFR), ionised calcium, 25-hydroxyvitamin D, and a panel of bone turnover markers.

RESULTS

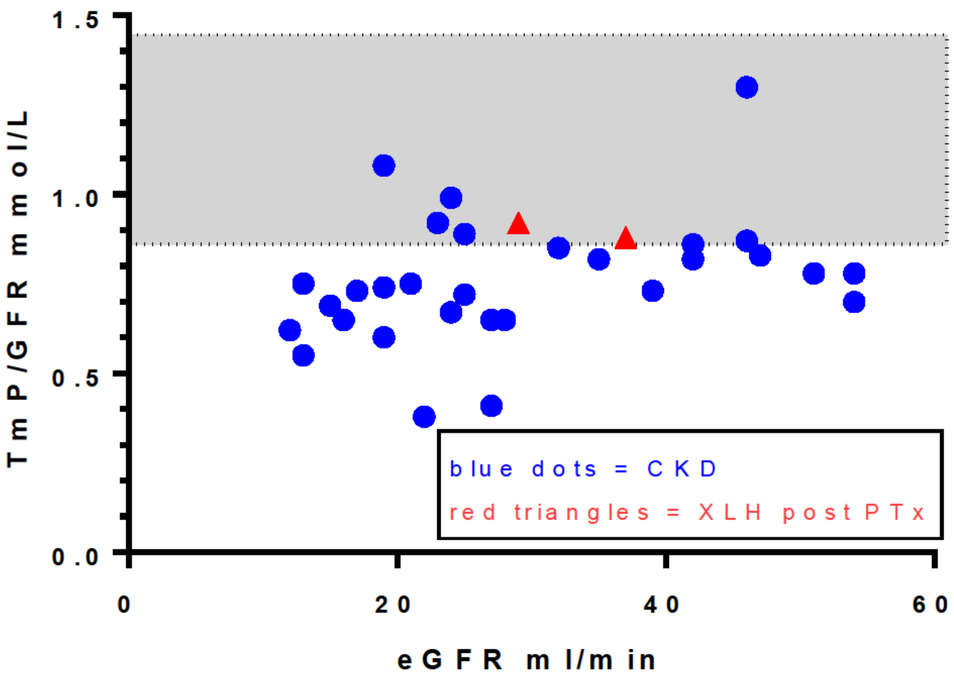
Relationship Between eGFR and FGF23



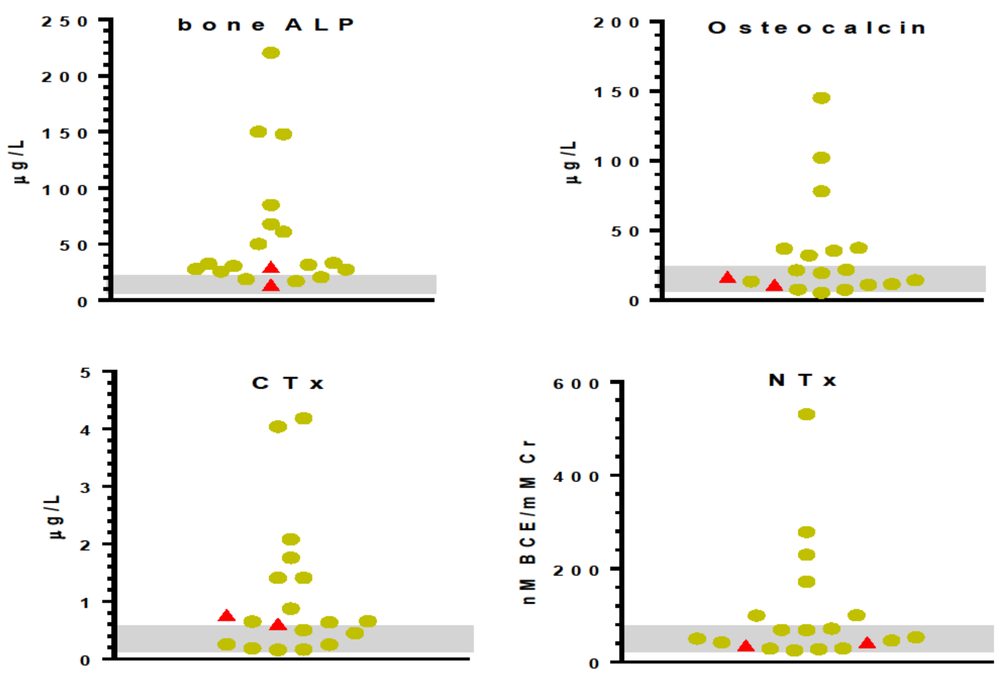
Relationship between FGF23 and TmP/GFR



Relationship Between eGFR and TmP/GFR



Bone Turnover Markers in XLH including 2 Cases of XLH and Hypoparathyroidism (red dots)



CONCLUSIONS

It is not possible to develop hypophosphatemic bone disease in the setting of FGF23 excess unless PTH is present. FGF23 resistance is extant when PTH is absent.

References

Crowley RK, Kilbane M, King TF, Morrin M, O'Keane M, McKenna MJ. Hungry bone syndrome and normalisation of renal phosphorus threshold after total parathyroidectomy for tertiary hyperparathyroidism in X-linked hypophosphataemia: a case report. J Med Case Rep. 2014;8(1):84.

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