

X-linked Hypophosphatemia in Pregnancy: Case Series with Management Outline

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Introduction

Familial X-linked hypophosphataemia rickets¹

- Rare inherited condition of bone metabolism
- Affects 1 in 20,000 individuals
- Caused by a mutation in the PHEX gene resulting in
 1. Excess production of FGF23 and thus (2)
 2. Excessive urinary excretion of phosphate
- 50% risk of transmission to offspring

Bone metabolism

- Interactions between PTH, calcitonin and VitD as depicted in image 1
- Role of FGF23 in calcium homeostasis was only recently discovered
 - its function is to prevent VitD mediated hyperphosphatemia
 - Net effect of FGF23 is to decrease phosphate²

Pregnancy

- Is a period of increased calcium requirement to encourage growth of foetal tissues
- Most of calcium and phosphate transport occurs in the third trimester against a concentration gradient².

Aim:

Case series of two sisters with XLH followed up during pregnancy at Medway Hospital from *October 2021 to December 2022* with an aim to highlight the management and outcome of this rare condition in pregnancy.

Design and Methodology

Timescale: October 2021 to December 2022

Methods: Electronic records of their pregnancies were reviewed, including antenatal clinics, emergency presentations and admissions as well as delivery outcomes.

Analysis: Excel was used for calculations. Results and management compared to PubMed literature using search words.

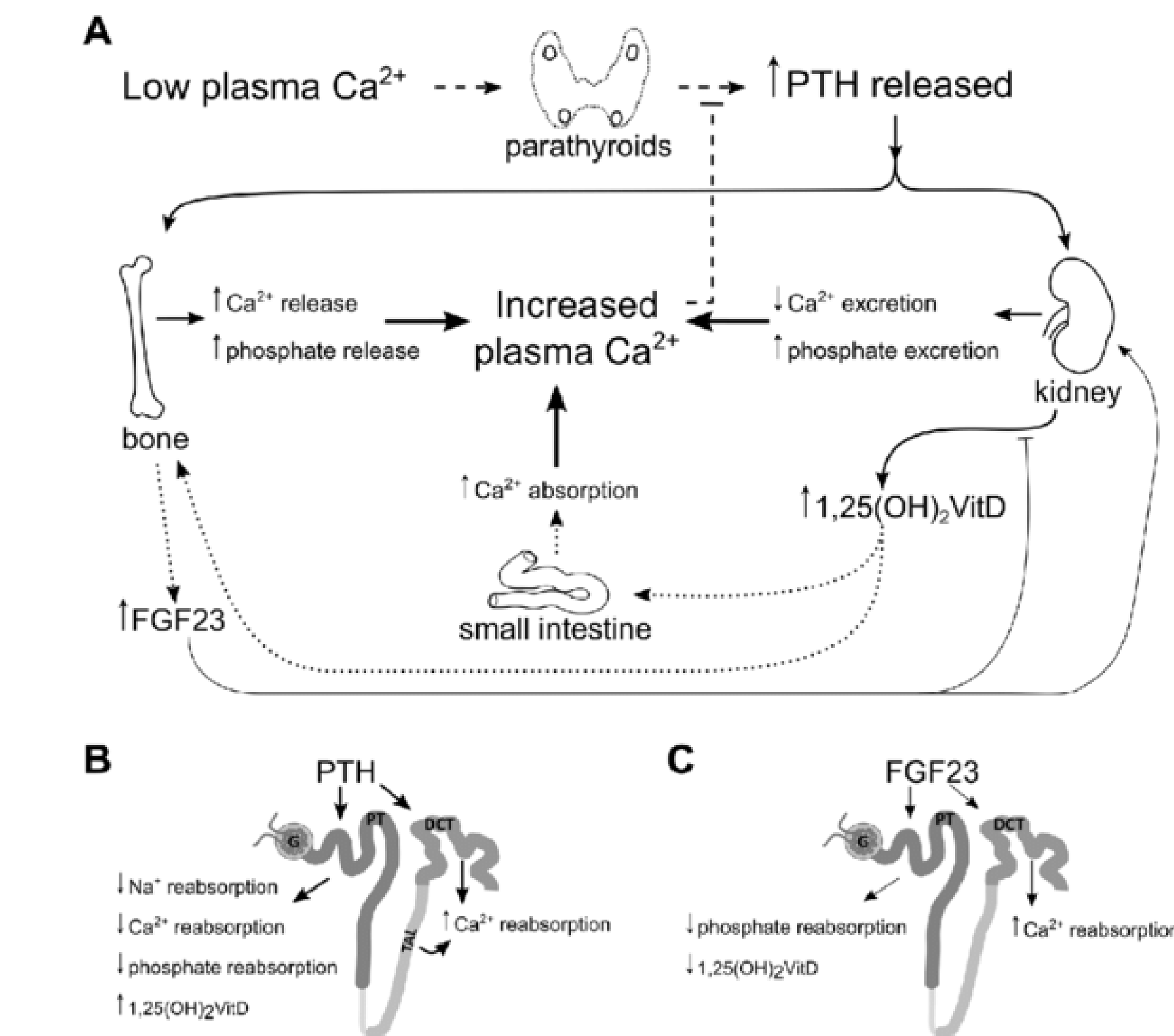


Image 1: Role of PTH and newly discovered FGF23 in bone metabolism³

Results

- Booking phosphate levels 0.34mmol/L and 0.4mmol/L

Antenatal planning

- **Medication**: Alfacacidol, PO Phosphate & Aspirin 150mg due to high risk of IUGR.
- **Serum phosphate levels** measured every 3wks in first two trimesters and weekly during third trimester (trends shown in graph 1)
- **Additional fetal growth scans** on weeks 28, 32 and 36wks

3rd trimester and intrapartum care

- During 3rd trimester IV phosphate replacement was used.
- Parenteral phosphate was also used intrapartum requiring MCU admission to monitor electrolytes.

Delivery

- Pre-delivery **levels of phosphate** were **0.52 mmol/L** in both cases.
- **Planned delivery method at 37wks** by **elective uncomplicated caesarean section** due to the associated rickets bony pelvis affection (Rachitic Pelvic Osteo-dystrophy).
- Outcomes
 - First delivered at 36 weeks+3 due to resistant hypophosphatemia with a baby weight 2920 g.
 - The second delivered at 37 weeks+2 with baby weight 2725 g.

Demographics

- 24yo G2P1 with previous EMCS. PMH of osteomalacic metatarsal stress fractures
- 18yo G1, no co-existing complications

Protocol for IV phosphate replacement

- 1) Admission to MECU and overnight stay
- 2) IV infusion of Monofer iron
- 3) Followed by an *infusion pump of 30mmol of phosphate infusion over 12hrs with a maximum infusion rate of 10 mmol/hr* to avoid hypocalcaemia.
- 4) Four hourly VBGs were performed to monitor calcium levels.
- 5) Overnight stay and repeat bloods next morning with aim of phosphate > 0.3 mmol/L

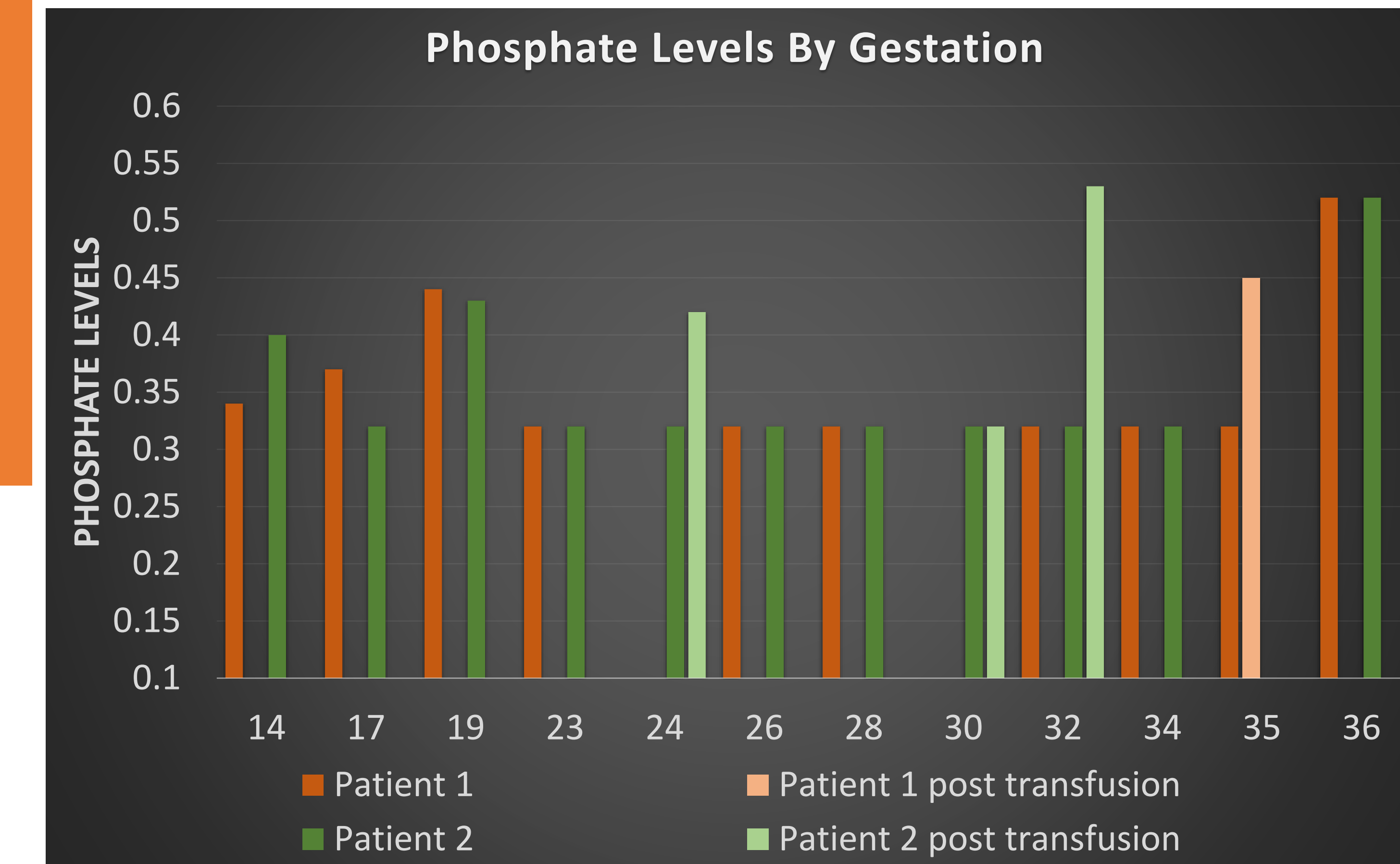
In the case of resistant hypophosphataemia, the reinfusion included IV phosphate 50mmol over 12hrs using infusion pump at rate of 10 mmol/hr.

Conclusions

- Two relatives with XLH-Rickets managed at Medway Maternal-Medicine-Centre with Endocrinology Input with good neonatal and maternal outcome.
- Regular blood tests for serum phosphate levels and additional growth scans performed
- Aim to keep IV phosphate use limited for third trimester to reduce risk of hypocalcaemia
- Increased demand of phosphorus in 3rd trimester is in keeping with literature⁴
- Delivery via ELCS
- Limited previous literature demonstrated similar management⁵

Limitations

1. No control of confounding factors
2. Small number of participants / difficult to generalise results
3. Young age of participants
4. No guidelines for requirement of IV phosphate; thus, clinical judgement had to be used.
5. Limited literature to compare



Graph 1: Blood phosphate levels throughout pregnancy including pre- and post- transfusion levels where relevant

References

(1) NORD (National Organization for Rare Disorders). (n.d.). *Familial Hypophosphatemia*. [online] Available at: <https://rarediseases.org/rare-diseases/familial-hypophosphatemia/> (2) Fiander, A., Baskaran Thilaganathan and College, R. (2015). Your essential revision guide : MRCOG part one : the official companion to the Royal College of Obstetricians and Gynaecologists revision course. London: Cambridge University Press. (3) Lee, J.J., Plain, A., Beggs, M.R., Dimke, H. and Alexander, R.T. (2017). Effects of phospho- and calciotropic hormones on electrolyte transport in the proximal tubule. *F1000Research*, 6, p.1797. doi:<https://doi.org/10.12688/f1000research.12097.1>. (4) Kovacs, C.S. (2016). Maternal Mineral and Bone Metabolism During Pregnancy, Lactation, and Post-Weaning Recovery. *Physiological Reviews*, 96(2), pp.449–547. doi:<https://doi.org/10.1152/physrev.00027.2015>. (5) Shonibare, T. and Yamoah, K. (2019). Management of Familial Hypophosphatemia in Pregnancy. *Endocrine Abstracts*. doi:<https://doi.org/10.1530/endoabs.65.p100>.