

Normocalcemic Hyperparathyroidism in Children

Dimitrios T. Papadimitriou¹, Eleni Dermitzaki¹, Kleantes Kleantous¹,
Anastasios Papadimitriou², George Mastorakos³

1. Pediatric Endocrine Clinics, Athens Medical Center, Greece
2. Attikon University Hospital, Haidari, Greece,
3. Areteio Univeristy Hospital, Athens, Greece.

No disclosures

Background

- Childhood and adolescence are the critical periods for the establishment of lifelong bone health.
- **Normocalcemic primary hyperparathyroidism (NPHPT)** has been recognized as a variant of primary hyperparathyroidism (PHPT) 15 years ago, characterized by elevated PTH level with persistently normal concentrations of albumin-adjusted total and ionized calcium, in the absence of secondary causes of hyperparathyroidism
- and related to **increased risk in development of osteopenia or osteoporosis as well as development of parathyroid adenoma (15%) and hypercalcemia-hypercalciuria with renal consequences.**

Aim

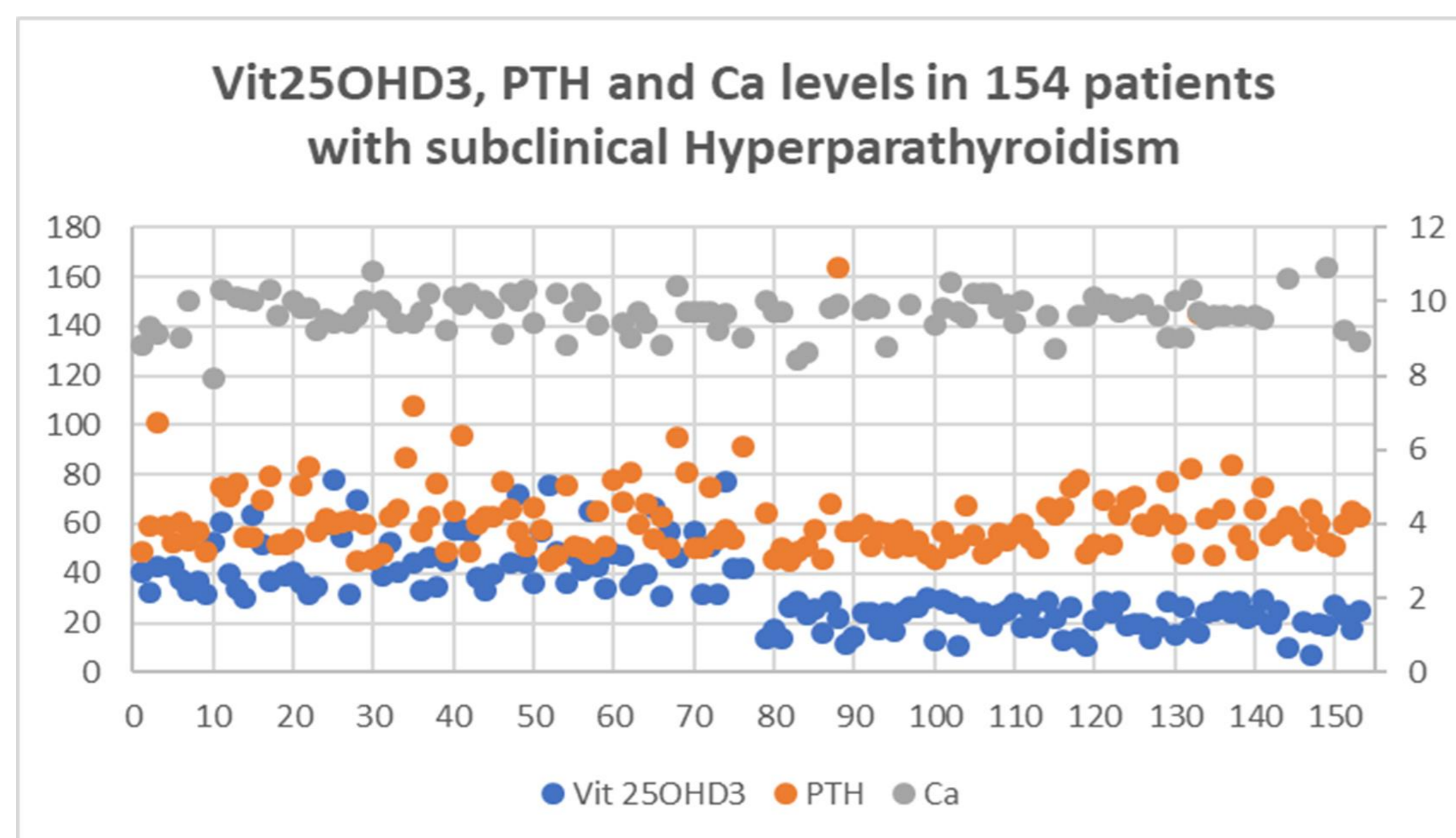
To identify and correct biochemical disorders of PTH in normocalcemic children

Methods

We performed in all patients that visited our pediatric endocrine unit for two years (1-Nov 2016 until 31-Oct 2018), a complete calcium metabolism evaluation (Ca, P, ALP, 25OHD, intact PTH).

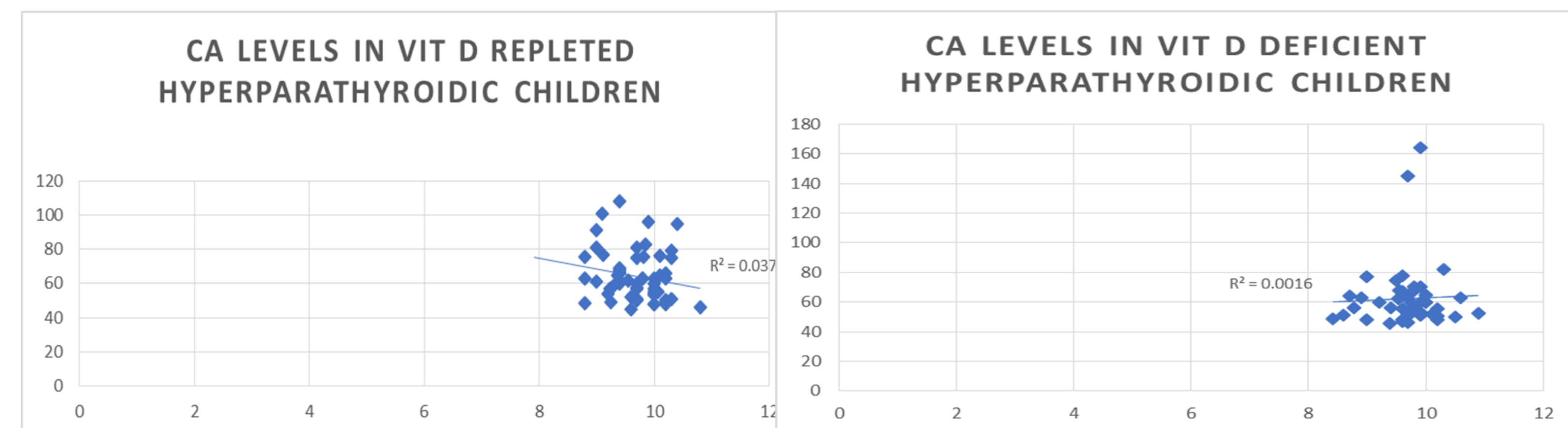
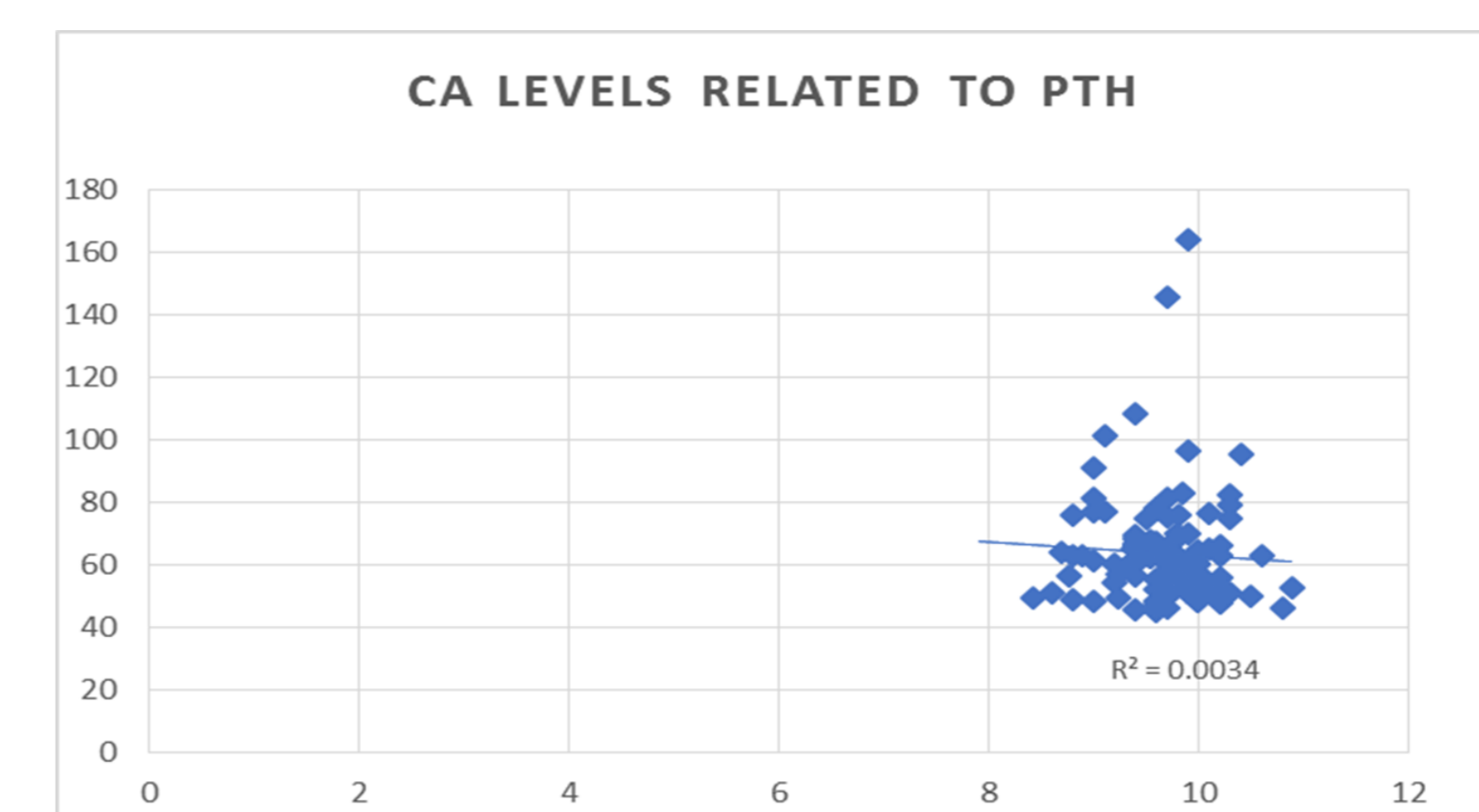
Results & Interventions

- A total of **3060 patients** - excluding those that consulted for vitamin D deficiency, Ca metabolism abnormalities or known renal pathology (i.e. Bartter syndrome)
- We identified 154 patients: **5.1% with hyperparathyroidism: PTH > 45 pg/ml**, (Horm Res Paediatr 2015;84:124-129) and normal total serum calcium levels:
 - **51 % of them were vitamin D replete** (25OHvitD >30 ng/ml, group 1)
 - **49 % were vitamin D deficient** (25OHvitD <30 ng/ml, group 2).
- All patients were treated with **cholecalciferol (8000-16000 IU daily)+calcium supplementation 1000 mg/day.**
- Evaluation of calcium metabolism (Ca, P, ALP, 25OHD, 1,25OHD, PTH) was performed every 3 months.



- **In 6 patients** (4 from group 1 and 2 from group 2) **elevated PTH did not respond to 6 months** of combined cholecalciferol/calcium therapy
- These patients were **switched to the non-calcemic synthetic 1-25(OH)2-vitamin D analogue, paricalcitol**, at the dose of 2 mcg x 1-3/day
- Evaluation of calcium metabolism (Ca, P, ALP, 25OHD, 1,25OHD, PTH, urine Ca/Cr) was performed every 3 months.

Parathormone levels normalized in 5 patients by 3 months of treatment and in 1 by 10 months of treatment, with calcium in serum and urine (Ca/Cr morning 2-hr sample) being within normal range for age during treatment in all patients.



Discussion and Conclusions

- The **incidence of normocalcemic hyperparathyroidism** in childhood is **high**
- **In all normocalcemic children checked for vitamin D, concomitant measurement of PTH is required**
- **Most of the cases** seem to be secondary hyperparathyroidism as they are **resolved with administration of cholecalciferol and calcium**
- Even in cases with vitamin D sufficiency, PTH fell to normal after administration of cholecalciferol and calcium
- This probably means that **vitamin D sufficiency may not be for everybody a level > 30 ng/ml** and that Calcium intake plays also a crucial role
- **In the 6 cases that did not respond** to therapy with cholecalciferol and calcium, **hyperparathyroidism seems to be either primary or tertiary**
- Even in primary hypercalcemic hyperparathyroidism, PTH is improved when Vitamin D levels are restored

Vitamin D repletion in patients with primary hyperparathyroidism and coexistent vitamin D insufficiency. J Clin Endocrinol Metab. 2005
- Vitamin D suppresses PTH gene expression and reduces parathyroid cell proliferation

Primary hyperparathyroidism and the skeleton Clin Endocrinol (Oxf). 2008 Jul
- Subclinical hyperparathyroidism **PTH>45 pg/ml** should be **treated with cholecalciferol (8000-16000 IU/day) + calcium** supplementation (1000 mg/day), but since studies in primary hypercalcemic hyperparathyroidism have shown that high dose cholecalciferol may worsen calciuria,

Biochemical effects of calcifediol supplementation in mild, asymptomatic, hyperparathyroidism with concomitant vitamin D deficiency. Endocrine. 2009;36:305-310
- we propose to **switch to paricalcitol 2-6 mcg/day, if PTH is unresponsive to cholecalciferol and calcium treatment** after a minimum of 3 months
- **Paricalcitol treatment normalizes PTH, protecting bone and general health**
- Further studies are needed to standardize this approach.