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# Poster Presentations: Calcium and Bone

**P213****Epidemiology of primary hyperparathyroidism in Santander, Spain**

Laura Ramos<sup>1</sup>, Pedro Muñoz<sup>2</sup>, María Piedra<sup>1</sup>, Luis Vazquez<sup>1</sup> & Jose Antonio Amado<sup>1</sup>

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**Background and aims**

Primary hyperparathyroidism (PHPT) is a common endocrine disorder with different epidemiological patterns among countries. The incidence of PHPT is unknown in Spain. The aim of our study is to assess the prevalence and incidence of diagnosed PHPT in adults between 1970 and 2014 in Santander, a population of 290.000 inhabitants, located in the north of Spain.

**Subjects and methods**

All patients diagnosed with primary hyperparathyroidism from 1970 to 2014 were included. PHPT was diagnosed when persistent hypercalcemia occurred with the presence of elevated or inappropriately normal parathyroid hormone levels. Prevalence and incidence density adjusted for age and sex were calculated for each 5-year period.

**Results**

We identified 709 patients (82.3% females) diagnosed with PHPT by the end of 2014. Females were older than males at baseline (median age 67.6 years (57.8–75.9) and 63.7 years (52.1–74.2) respectively) ( $P < 0.05$ ). Prevalence of PHPT was higher in females, and the female preponderance increased with age. In the mid-1990s the incidence rate in women was 3.72/100.000 person-years and doubled in the period 1995-1999, with an incidence rate of 8.38/100.000 person-years. Incidence increased in the following years, and in the period from 2005 to 2009, it doubled again from 12.08/100.000 person-years in 2000 to 2004 to a maximum level of 24.52/100.000 person-years in the period from 2005 to 2009. In the last period of study, from 2010 to 2014, the incidence in women decreased up to 21.44/100.000 person-years. The increased incidence is progressive and less flashy in males than females. The incidence in the period from 1995 to 1999 was 2.75/100.000 person-years and doubled in the period from 2010 to 2014, becoming 5.20/100.000 person-years. The prevalence of diagnosed PHPT in Santander increased from 0.01 per 1000 population in the period from 1980 to 1984 to 0.38 per 1000 population in the period from 2010 to 2014.

**Conclusions**

The incidence of PHPT in Santander continues its remarkable rise. The incidence of diagnosis is greater in females than in males and increases with age. The overall increase in incidence may be the result of more frequent plasma calcium measurements, periods of increasing medical interest or environment factors. However, the most likely explanation is the bias of the selective detection of PHPT in patients who are being evaluated for osteoporosis.

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**P214****Human Chorionic Gonadotrophin (hCG) as a diagnostic test to differentiate between Parathyroid Carcinoma, Primary Benign Hyperparathyroidism and Secondary Hyperparathyroidism.**

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**Introduction**

Parathyroid carcinoma (PCa) is a rare presentation of primary hyperparathyroidism (PHPT), accounting for less than 1% of cases. Differentiating parathyroid cancer from benign hyperparathyroidism is clinically challenging. Some previous work suggest that there is a paraneoplastic hCG production in parathyroid cancer (Stock et al 1987, Rubin et al 2008). In this study, we aimed to investigate whether the hCG +  $\beta$  kit from Roche Diagnostics could distinguish PCa patients from primary and secondary hyperparathyroidism. Additionally, we validate hCG levels according to renal function and determine hCG test sensibility and specificity to diagnose parathyroid cancer.

**Material and methods**

We studied a series of eight patients suffering from advanced PCa, referred to the CHU de Liege. A group of 20 PHPT patients and 25 patients with secondary hyperparathyroidism (SHP) due to chronic renal failure were used as controls. hCG +  $\beta$  kit on Cobas (Roche Diagnostics) uses 2 monoclonal antibodies that recognize holo-hCG, nicked hCG,  $\beta$ -core fragment and free  $\beta$ -subunit. Limits of hCG detection and quantification are  $< 0.1$  and  $< 0.6$  mUI/ml. In non pregnant and postmenopausal women and in men, hCG (p95) is  $< 1$  (5.3),  $< 7$  mUI/ml (8.3) and  $< 2$  (2.6) mUI/mL, respectively.

**Results**

The 8 PCa patients (3 women) presented high serum hCG values at: 1.29, 3.46, 5.7, 24.2, 31.2, 34.1, 36.5 and 164 U/I. Values of 1.29 and 3.46 were obtained in 2 postmenopausal women. The lowest value was presented by the only still alive patient who had hormonal and biochemical normalization and tumor shrinkage induced by anti-parathyroid hormone immunotherapy (Beta et al. 2004). In cancer patients, there was a significant correlation ( $r = 0.786$ ;  $P < 0.05$ ) between hCG and PTH whereas median hCG (5.7 U/I) was significantly higher than in PHP (1.25 U/I) and SHP (0.97 U/I). hCG test sensitivity was 75% and specificity was 94% to detect parathyroid cancer, with a cut-off of hCG of more than 5.68 U/I.

**Conclusions**

These results suggest that serum hCG might have the potential to discriminate between parathyroid adenomas and carcinomas, with a sensibility of 75% and a specificity of 94%. The only patient still alive who underwent a PTH immunotherapy, presented the lowest hCG values. If hCG could be predictive of PCa survival needs to be studied in a larger series of patients. A future area of research revealed by this data is to test hCG immunotherapy in parathyroid cancer.

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**P215****Reliability of serum Calcium to Phosphorus (Ca/P) ratio as an accurate and inexpensive tool to define disorders of Ca-P metabolism: preliminary data**

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**Background**

Primary hyperparathyroidism (PHPT) is the third most common endocrine disorder. The Ca/P ratio is an accurate tool to differentiate patients with PHPT ( $> 3.5$  if Ca and P are expressed in mg/dl) from healthy subjects [1]. The reliability of this index is based on the fact that serum Ca and P are inversely related together. However, other disorders of the Ca-P metabolism, such as hypophosphoremia (HypoP), might impair the Ca/P ratio.

**Aim**

To validate the accuracy of Ca/P ratio in the diagnosis of Ca-P metabolism disorders, including also patients with documented HypoP.

**Methods**

A single-center, retrospective, case-control study was carried out, including 130 patients with documented PHPT and 300 patients with HypoP, compared with 120 controls. HypoP patients were enrolled among HIV-infected patients on HAART treatment from the large Modena cohort. The main outcome measures were: serum Ca, P, parathyroid hormone (PTH), 25-OH vitamin D, albumin and creatinine.

**Statistical analysis**

Comparisons among groups were performed by the nonparametric Kruskal-Wallis, followed by the Dunn's post hoc test. The diagnostic accuracy of Ca/P ratio was investigated by receiver operator characteristics (ROC) curves in order to define cut-off points (with the highest sensitivity and specificity).

**Results**

The Ca/P ratio was significantly higher in the group of PHPT together with HypoP, compared to controls ( $P < 0.0001$ ). Also Ca and PTH were significantly different among groups, in particular they were higher ( $P < 0.0001$ ) in PHPT than both controls and HypoP, as expected. At ROC curves analysis, the cut-off of 3.6 for Ca/P ratio was able to identify patients with PHPT and HypoP (sensitivity 91%; specificity 93%). Among patients with Ca/P ratio above 3.6, the thresholds of 10.2 mg/dl for serum Ca (sensitivity 91%; specificity 98%) and of 83.6 pg/ml for PTH (sensitivity 92%; specificity 93%) were defined for the specific diagnosis of PHPT.

**Conclusions**

In this study we confirm the role of serum Ca/P ratio as a reliable index to diagnose a Ca-P metabolism disorder, especially PHPT and HypoP. In clinical practice, when a Ca/P ratio above 3.6 is found, the presence of serum Ca  $> 10.2$  mg/dl or PTH  $> 83.6$  pg/ml is able to discriminate patients with PHPT from those with HypoP.



## Reference

1. Madeo *et al*, Serum Calcium to Phosphorous (Ca/P) Ratio Is a Simple, Inexpensive and Accurate Tool in the Diagnosis of Primary Hyperparathyroidism. *JRBM Plus*, 2017. DOI: 10.1002/jbm.4.10019.

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## P216

### Secondary hyperparathyroidism after obesity surgery is associated with serum levels of 25-hydroxyvitamin D and ionized calcium

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## Background

Secondary hyperparathyroidism (SHPT) is common in obesity, and a concern after obesity surgery due to negative impact on bone. Longitudinal data is sparse, and relationships with vitamin D and calcium levels are unclear. We studied the prevalence of SHPT over five years after Roux-en-Y gastric bypass (RYGB) and investigated whether SHPT was associated with serum levels of 25-hydroxyvitamin D (25(OH)D) and ionized calcium (iCa).

## Methods

347 of 568 (61%) patients attending a 5-year follow-up visit after a RYGB at Oslo University Hospital in the years 2004-2008 were eligible for study inclusion. We excluded 14 patients with missing data, four with primary hyperparathyroidism and 10 with elevated serum creatinine. We defined SHPT as PTH > 7.0 pmol/l and vitamin D deficiency as 25(OH)D < 50 nmol/l. Low iCa refers to serum levels < 1.21 mmol/l (lower tertile of reference range or below). Substitution of vitamin D3 (1000 IE/day) and calcium carbonate (1000 mg/day) was recommended.

## Results

Among the 319 included patients (230 women) the prevalence of SHPT was 32% before surgery, while the prevalence was 18%, 24%, 28% and 35% after a half, one, two and five years, respectively. Vitamin D deficiency was found in 45% preoperatively, and 18%, 20%, 28% and 33% after a half, one, two and five years. The proportion with serum iCa in the lower range was: 24% preoperatively, and 29%, 35%, 44% and 49% at a half, one, two and five years. Table 1 illustrates the prevalence of SHPT by serum vitamin D and calcium levels (\*illustrates  $P < 0.001$  between subgroups).

Table 1

	Baseline	1/2y	1y	2y	5y
<b>25(OH)D (nmol/l)</b>					
<50	40	34	29	45	39
≥50	26*	13*	20*	19*	33 <sup>ns</sup>
<b>Ionized calcium (mmol/l)</b>					
<1.21	46	21	30	35	46
≥1.21	26*	16*	22*	22*	23*

## Discussion

The prevalence of SHPT decreased the first half year after RYGB and thereafter increased over time. SHPT was higher in vitamin D deficiency and with iCa levels in the lower range. Improved vitamin D and calcium status may potentially reduce the prevalence of SHPT both preoperatively and after obesity surgery.

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## P217

### The frequencies of persistent hyperparathyroidism and hypercalcemia after kidney transplantation: a single-center experience

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Bone mineral disorders usually resolve after successful kidney transplantation. Serum calcium (Ca), phosphorus (P) and parathyroid hormone (PTH) levels tend to normalize within time. Serum Ca levels > 10.2 mg/dL and PTH levels > 150 pg/mL at 6th–12th months of transplantation is defined as persistent

hypercalcemia and persistent hyperparathyroidism (PHPT) in recipients with normal graft function. Reported persistent hypercalcemia prevalence varies in wide range between 5% and 66%. This huge variation might be explained with different diagnostic criteria, heterogenic recipient population and variation in renal replacement vintage. We aimed to evaluate the prevalence of hypercalcemia and PHPT among recipients after successful kidney transplantation in our center.

## Methods

We performed a retrospective study involving a total 391 (224 males, 40.6 ± 11.9 years) adult kidney transplant recipients between January 2008 and December 2014. Recipients who were underwent parathyroidectomy before transplantation were excluded. Demographic and laboratory data of 307 recipients who were followed up at least 12 months were obtained by review of electronic file system. PHPT was defined as serum corrected Ca level > 10.2 mg/dl (at least twice in a 6 month period) and PTH > 150 pg/ml at 6th month of transplantation. Serum creatinine, Ca levels at pre- and post-transplant 1st, 3rd, 6th, 12th months, PTH levels at pre- and post-transplant 6th, 12th months of recipients were recorded.

## Results

A total 307 recipients (150 deceased, 157 living donor; 175 male, 132 female; mean age 39.4 ± 11.4 years) were enrolled the study. The mean duration of renal replacement treatment was 75.1 ± 3.3 months. Mean serum Ca levels before transplantation and at 1st, 3rd, 6th, 12th months of transplantation were 9.3 ± 0.8 mg/dl, 9.3 ± 0.7 mg/dl, 9.6 ± 0.7 mg/dl, 9.7 ± 0.7 mg/dl, 9.7 ± 0.7 mg/dl; and prevalence of hypercalcemia (> 10.2 mg/dl) at 1st, 3rd, 6th, 12th months of transplantation were 10.8%, 21.2%, 21.2% and 21.2%, respectively. Mean serum PTH levels before transplantation and at 6th, 12th months of transplantation (> 150 pg/ml) were 526.2 ± 474.9 pg/ml, 237 ± 334 pg/ml, 215 ± 236.9 pg/ml, and prevalence of hyperparathyroidism at 6th, 12th months of transplantation were 57.1% and 52.3%, respectively.

## Conclusion

PTH levels decreased and Ca levels remained stable after transplantation within 12 months in our study. Although prevalence of hyperparathyroidism was high, persistent hypercalcemia affected fewer recipients.

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### Prevalence and clinico-epidemiology of vitamin D deficiency in patients with type 2 diabetes mellitus and hypertension – a Pan-India study

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## Introduction

Vitamin D (vitD) deficiency is a worldwide epidemic health problem, with a prevalence of about 70–100% in general Indian population. The objective of this cross-sectional, clinico-epidemiological, Pan-India study was to evaluate the prevalence of vitD deficiency in patients with Type-2 diabetes mellitus (T2DM) or hypertension (HT) or both T2DM and HT and to understand the management practices in Indian real-world setting.

## Methods

Adults with a diagnosis of T2DM or HT or both (established/newly diagnosed), visiting physician for routine check-up, were enrolled. Percentage of patients with vitD deficiency in those with T2DM/HT/or T2DM + HT and prevailing management practices were assessed. VitD insufficiency and deficiency was defined as serum 25(OH)D levels 21–29 ng/ml and ≤ 20 ng/ml, respectively.

## Results

A total of 1501 (99.5%) patients completed the study (T2DM:500 [99.2%]; hypertension:499 [99.6%]; both T2DM and HT: 502 [99.8%]). Mean (± s.d.) age of the study population was 52.9 ± 12.49 years. Mean age at diagnosis of vitD deficiency was 52.5 ± 10.77 years; mean vitD level at the time of diagnosis was 16.9 ± 12.78 ng/ml. Overall prevalence of patients with low vitD levels (vitD deficiency and insufficiency) was 1257 (83.7%); 1231 (82%) were newly diagnosed cases. Out of 1257 (83.7%) patients with low vitD levels, 60.9% patients had vitD deficiency and 22.9% patients had vitD insufficiency. Prevalence of low vitD levels amongst patients with T2DM (n=500), HT (n=499) and T2DM + HT (n=502) was 84.2%, 82.6% and 84.5%, respectively. Out of 1257 patients with low level of vitD, 84.8% received vitD supplementation. Preferred dose of vitD was 60,000IU (70.2%); route of administration was oral for majority of patients (79.6%). Preferred frequency of

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