

Correlation of intact parathormone levels with serum calcium, serum phosphorus and serum vitamin d levels in surgical patients

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Abstract

Aim: The aim of our study was to determine a correlation between hyper parathyroidism and Serum Calcium, Phosphorus and Vitamin D levels. **Study Design:** A Hospital based cross-sectional study was conducted on the patients attending the Outpatient Department of Surgery, of SGRR Medical College, Dehradun (UK), during a period of 6 months from November 2016 to April 2017. A total number of 66 cases (32 male + 34 female) and 45 controls (20 male + 25 female) in the age group of 20-60 years were selected randomly for this study. Exclusion criteria were age less than 20 years and more than 60 years, pregnancy, diabetes, tuberculosis etc. **Methodology:** The blood samples were collected in fasting state and Serum iPTH, Vitamin-D, Calcium & Phosphorus levels were estimated on a fully automated machine 5600 of Ortho diagnostics. **Results:** The levels of iPTH were found to be higher in female cases than male cases and much higher when compared with controls both male & female. Both male & female hyper parathyroid cases were normocalcemic. Vitamin D levels were found to be lower in both male & female cases as compared to their normal counterparts. Serum Phosphorus levels were found to be on the lower side in both cases as compared with normal controls.

Keywords: Parathormone, Vitamin D, Calcium, Phosphorus.

Introduction

Parathyroid hormone is secreted by parathyroid gland that is important for bone remodeling, which is an ongoing process in which bone tissue is alternately resorbed and rebuilt over time. It increases blood calcium levels. The chief cells of the parathyroid glands secrete it as a polypeptide containing 84 amino acids, which is a prohormone. Parathormone essentially acts to increase the concentration of calcium in blood by acting upon parathyroid hormone 1 receptor, which is present at high levels in bone and kidney, and the parathyroid hormone 2 receptor that is present at high levels in the CNS, pancreas, testis and placenta [1]. Parathormone regulates Sr. Calcium through its effects on bone kidney and intestines [2]. Parathormone increases activity of 1- α hydroxylase enzyme, which converts 25-OH-cholecalciferol to 1,25 Dihydroxy cholecalciferol (the active form of vitamin D in kidney). Parathormone reduces the reabsorption of PO₄ from the proximal tubule of the kidney [3].

The most wellknown function of Vitamin D/ Parathormone axis is to maintain extracellular Calcium homeostasis [4]. Vitamin D, obtained largely from exposure to U.V B radiation and to a lesser extent from dietary and supplemental sources, increases the efficiency of intestinal calcium absorption, while parathormone is released in response to low circulating Calcium concentrations.

The release of Parathormone stimulates the reabsorption of Calcium in the kidney, the resorption of calcium from the skeleton and enhances the production of Calcitriol. Hypovitaminosis D is associated with increased parathormone secretion, increased bone turnover, Osteoporosis, Osteomalacia and an increased risk of fracture [5, 6, 7, 8].

Although the biological activities of Vitamin D are mainly manifested in the regulation of Calcium-Phosphorus metabolism, studies in the past 30 yrs indicate that vitamin D may play an important role in the immune system [9, 10].

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Data regarding the relationship between hyper parathyroidism and Vitamin D, Calcium and Phosphorus levels is scarce and relationship between particular causes has not been analyzed, so we thought of conducting this study.

Material & Method: A hospital based cross sectional study was conducted on patients attending the Outpatient Department of Surgery of SGRR Medical College, Dehradun (U.K.), during a period of 6 months from Nov 2016 to April 2017.

A total number of 66 cases (32 male + 34 female) and 45 controls (20 male+ 25 female) in the age group 20-60 years were selected randomly for the study. **Exclusion criteria** were age less than 20 yrs and more than 60 yrs, pregnancy, Diabetes, Tuberculosis etc.

Results

The serum iPTH levels were found to be high in both hyper parathyroid males ($208.88 \pm 167.01 \pm 29.59$ pg/ml) and hyper parathyroid females ($225.36 \pm 155.44 \pm 28.78$ pg/ml) as compared to normal males ($32.54 \pm 13.23 \pm 2.96$ pg/ml) and normal females ($23.09 \pm 1.88 \pm 0.38$ pg/ml) respectively, p value was found to be < 0.0001 which is highly significant. The serum iPTH levels were only slightly high in cases of hyper parathyroid female cases as compared to hyper parathyroid males, p value was not significant.

Both male and female hyper parathyroid cases were normocalcaemic ($9.85 \pm 1.44 \pm 0.25$ mg/dl) and ($10.04 \pm 1.04 \pm 0.19$ mg/dl) respectively, p value was not significant.

Vitamin D levels were found to be much lower in both male ($12.52 \pm 1.09 \pm 0.20$ ng/ml) and female ($11.75 \pm 3.36 \pm 0.62$ ng/ml) hyper parathyroid cases as compared to normal males ($27.05 \pm 11.25 \pm 2.50$ ng/ml) and normal females ($19.52 \pm 6.05 \pm 1.21$ ng/ml) p value was found to be < 0.0001 which was highly significant. The serum vitamin D levels were only slightly high in cases of hyper parathyroid male cases as compared to hyper parathyroid female, p value was not significant.

Serum Phosphorus levels were found to be on the lower side in both male cases ($2.80 \pm 0.73 \pm 0.13$ mg/dl) and female cases ($2.81 \pm 0.39 \pm 0.07$ mg/dl) as compared with normal male controls ($32.54 \pm 13.23 \pm 2.96$ mg/dl) and female controls ($3.33 \pm 0.62 \pm 0.12$ mg/dl) respectively, p value was < 0.0007 which was highly significant.

There is almost no difference in the levels of Phosphorus in both male and female hyper parathyroid cases. Results are tabulated in Table (i) (ii) and (iii) and depicted graphically in Fig. 1, 2 & 3.

Table-1: Comparison of male hyper parathyroid cases with their controls.

Parameters	Males		t-value	P-value	Significant/ Non-significant
	Cases (32)	Control (20)			
iPTH	$208.88 \pm 167.01 \pm 29.59$ pg/ml	$32.54 \pm 13.23 \pm 2.96$ pg/ml	4.68	< 0.0001	Significant
Calcium	$9.85 \pm 1.44 \pm 0.25$ mg/dl	$9.68 \pm 0.67 \pm 0.15$ mg/dl	0.50	0.6178	Non-significant
Vitamin D	$12.52 \pm 1.13 \pm 0.20$ ng/ml	$27.05 \pm 11.28 \pm 2.50$ ng/ml	7.33	< 0.0001	Significant
Phosphorus	$2.80 \pm 0.73 \pm 0.13$ mg/dl	$3.52 \pm 0.62 \pm 0.14$ mg/dl	3.63	< 0.0007	Significant

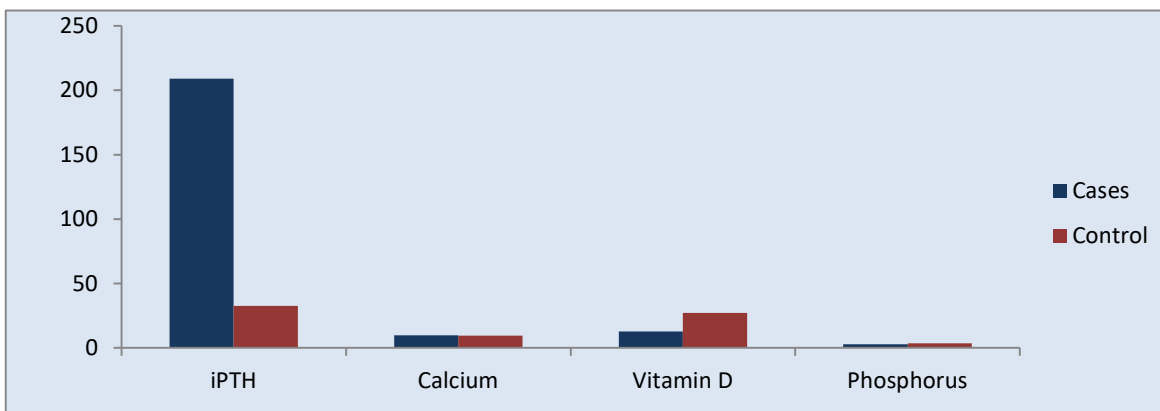


Figure-1: Comparison of male hyper parathyroid cases with their controls.

Table-2: Comparison of female hyper parathyroid cases with their controls.

Parameters	Females		t-value	p-value	Significant/ Non-significant
	Cases (34)	Control (25)			
iPTH	225.36±155.44±28.78 pg/ml	23.09±1.88±0.38 pg/ml	6.01	<0.0001	Significant
Calcium	10.04±1.04±0.19 mg/dl	9.94±2.54±0.51 mg/dl	1.41	<0.1580	Non- Significant
Vitamin D	11.75±3.36±0.62 ng/ml	19.52±6.05±1.21 ng/ml	6.15	<0.0001	Significant
Phosphorus	2.81±0.39±0.07 mg/dl	3.33±0.62±0.12 mg/dl	3.98	<0.0002	Significant

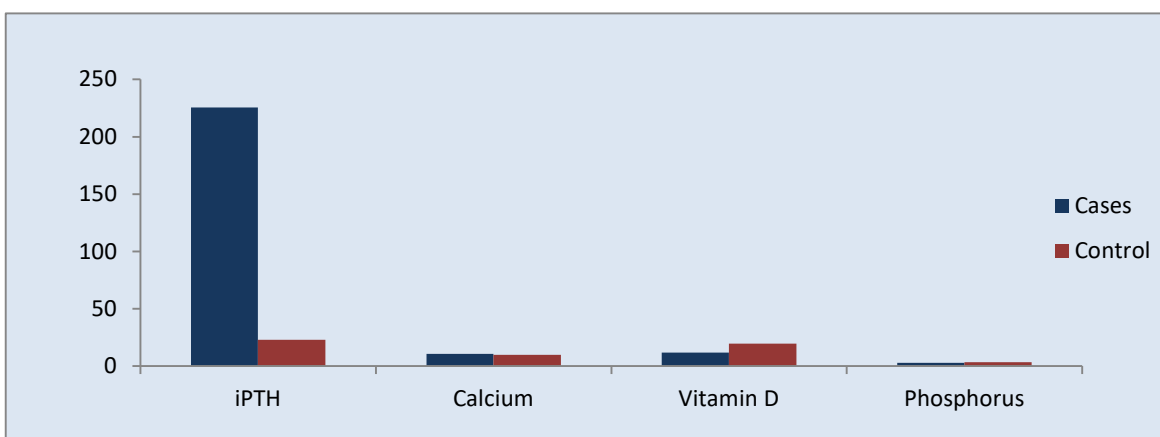


Figure-2: Comparison of female hyper parathyroid cases with their controls

Table-3 Comparison of male and female hyper parathyroid cases.

Parameters	Male Cases (32)	Female Cases (34)	t-value	P-value	Significant/ Non-significant
iPTH	208.88 ± 167.01 ±29.59 pg/ml	225.36±155.44±28.78 pg/ml	0.39	0.6911	Non-significant
Calcium	9.85±1.44 ±0.25 mg/dl	10.64±1.04±0.19 mg/dl	2.53	0.0137	Non-significant
Vitamin D	12.52±1.13±0.20 ng/ml	11.75±3.36±0.62 ng/ml	1.15	0.2534	Non-significant
Phosphorus	2.80± 0.73 ±0.13 mg/dl	2.81±0.39±0.07 mg/dl	0.06	0.945	Non-significant

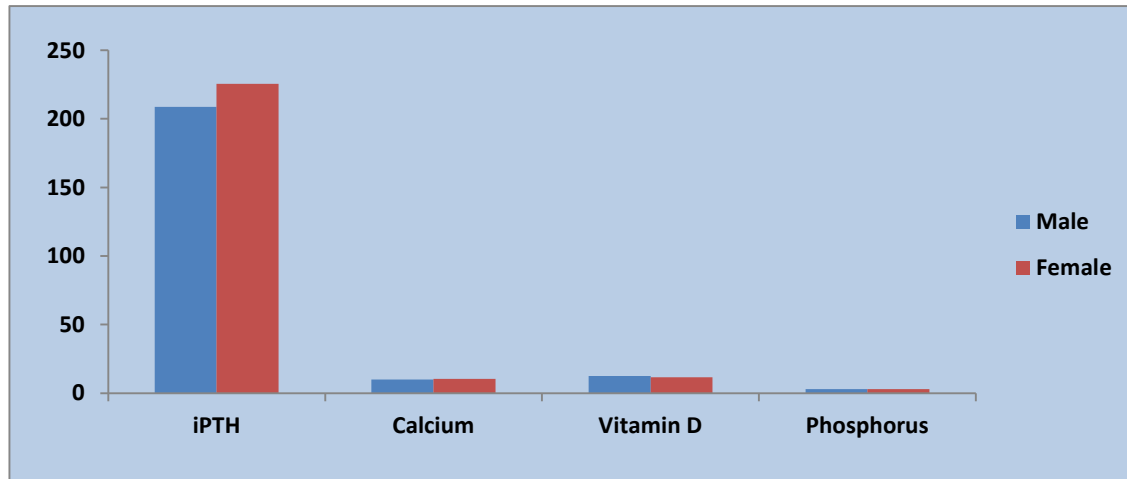


Fig-3: Comparison of male and female hyper parathyroid cases.

Discussion

According to the population-based surveys, hyper parathyroidism is now considered as the third most frequent endocrinopathy (after Diabetes mellitus and thyroid disease), with a prevalence of approximately 1/1000 in the general population [15].

In our study Vitamin D deficiency was the most common cause of elevated Parathormone levels in presence of normal serum calcium. Vitamin D deficiency is a well known cause of secondary Hyper parathyroidism [16]. An inverse relationship exists between 25OH Vitamin D and parathormone [17]. When Vitamin D decreases below the normal range, the parathyroid gland responds with increased synthesis and secretion of parathormone. However the mechanism by which Vitamin D deficiency increases parathormone levels is not clear, at least it does not seem to be mediated through serum calcium levels because serum calcium levels are normal and yet parathormone levels are elevated.

The diagnosis of Hyper parathyroidism is usually based on the measurement of serum calcium or parathormone levels [18]. Less obvious presentations such as normocalcaemic hyperparathyroidism is more and more frequently detected [19]. It is of note that, due to more systematic measurement of serum calcium, Hyper parathyroidism has shifted from a rare disease with severe bone and/or renal complications to a frequent, mostly asymptomatic disease.

Our study supports others which indicate the inverse correlation of Vitamin D and parathormone [20, 21, 22, 23] even though Kilicarslan, Cenoliaslan, and Gezgen [24] reported that in their study 75% of Vitamin D deficient patients had normal levels of parathormone.

Arabi et al stated that the negative relationship between vitamin D & parathormone is modulated by age but not by gender. Reports from the Middle Eastern countries indicate that an inverse relationship exists between vitamin D and parathormone levels in all age groups. [25]

Adrawi et al in their study found that the inverse relationship between vitamin D and parathormone was not influenced by the level of vitamin D and could not pinpoint the levels of vitamin D at which parathormone levels will plateau [26]. From the studies cited above, it appears that various factors play a role in raising the parathormone levels, but one important factor that increases the parathormone is a level of vitamin D below 20ng/ml. We also observed a strong inverse correlation of Phosphorus levels with hyper parathyroidism. Phelan et al found no relationship between parathormone above & below 300pg/ml and mortality. A low calcium levels, low phosphorus levels and a high Parathormone level seem to increase the risk of mortality. [27]

Limitation of the study is that analyses were based on observational data and therefore, no causal inference can be made from the study results. Another limitation was that results could not be stratified due to the relatively small sample size.

Conclusion

In conclusion we report the co-existence of Vitamin D deficiency and hyperparathyroidism, with depletion of vitamin D masking the biochemical diagnosis of hyper parathyroidism. Above all it will be of paramount importance to prescribe Vitamin D supplementation in order to increase the Vitamin D serum levels when it is

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initially low (even marginally). Patients started on Vitamin D therapy for low Vitamin D and elevated Parathormone levels, should be monitored periodically to ensure that Parathormone levels return to normal. If Parathormone remains elevated despite successful Vitamin D replacement, then hyperparathyroidism needs to be considered as a concurrent diagnosis.

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References

1. Physiology: 5/5 ch.6/S 5ch-11-Essentials of Human Physiology.
2. Coetzee M, Kruger MC. Osteoprotegerin-receptor activator of nuclear factor-kappa B ligand ratio: a new approach to osteoporosis treatment? *South Med J*. 2004 May; 97(5):506-11.
3. Gardener D, Shoback D (2011). *Green spans Basic & Clinical Endocrinology* (9thEdt.), McGraw Hill p232. ISBN 978-0-07-162243-1.
4. Silver J & Naveh-Many T. Vitamin D and the parathyroid. In *Vitamin D*. edn 2, Eds D Feldman. F Glorieux & J Wesley Pike. San Diego, Elsevier, 2004.
5. Lips P. Vitamin D deficiency and secondary hyperparathyroidism in the elderly: consequences for bone loss and fractures and therapeutic implications. *Endocr Rev*. 2001 Aug; 22(4):477-501.
6. Lips P, Netlembos JC, Jongen MJ et al, Histo-morphometric profile and Vitamin D status in patients with femoral neck fracture. *Metabolic Bone Disease and Related Research* 1982; 4: 85-93.
7. Kuchuk NO, Pluijm SM, van Schoor NM, Looman CW, Smit JH, Lips P. Relationships of serum 25-hydroxyvitamin D to bone mineral density and serum parathyroid hormone and markers of bone turnover in older persons. *J Clin Endocrinol Metab*. 2009 Apr;94 (4): 1244-50. doi: 10.1210/jc.2008-1832. Epub 2009 Jan 21.
8. Trivedi DP, Doll R, Khaw KT. Effect of four monthly oral vitamin D3 (cholecalciferol) supplementation on fractures and mortality in men and women living in the community: randomised double blind controlled trial. *BMJ*. 2003 Mar 1;326(7387):469.
9. Lemire JM, Adams JS et al. 1-alpha 25 dihydroxy vitamin D₃ suppresses proliferation and Immunoglobulin production by normal human peripheral blood mononuclear cells. *J Clin Investing*. 1984; 74:1451-55.
10. Rigby WF, Stacy T, Fanger MW. Inhibition of T lymphocyte mitogenesis by 1,25-dihydroxyvitamin D₃ (calcitriol). *J Clin Invest*. 1984 Oct;74(4):1451-5.
11. Armitage EK. Parathyrin (parathyroid hormone): metabolism and methods for assay. *Clin Chem*. 1986 Mar; 32 (3):418-24.
12. Lai JK, Lucas RM, Clements MS, Harrison SL, Banks E. Assessing vitamin D status: pitfalls for the unwary. *Mol Nutr Food Res*. 2010 Aug; 54(8): 1062-71. doi: 10.1002/mnfr.200900468.
13. Teitz. NW (ed). *Fundamentals of Clinical Chemistry* ed3. Philadelphia: WB Saunders; 705-713; 1987.
14. Teitz NW (ed). *Fundamentals of Clinical Chemistry*. Ed 3. Philadelphia: WB Saunders; 706-716; 1987.
15. Lundgren E, Hagstrom EG, Lundin J, Winner back KL, Ross J, Ljunghall S, et al. Primary hyperparathyroidism revisited in menopausal women with serum calcium in the upper normal range at population based screening 8 years ago. *World S Surg* 2002; 26(8): 931-6.
16. Cusano NE, Silverberg SJ, Bilezikian JP. Normocalcemic primary hyper parathyroidism. *J Clin Densitom*. 2013 Jan-Mar; 16(1): 33-9. doi: 10.1016/j.jocd.2012.12.001.
17. Heaney RP. The Vitamin D requirement in health and disease. *J Steroid Biochem Mol Biol*. 2005 Oct; 97 (1-2): 13-9. Epub 2005 Jul 18.
18. Eastell R, Arnold A, Brandi ML, Brown EM, D'Amour P, Hanley DA, Rao DS, Rubin MR, Goltzman D, Silverberg SJ, Marx SJ, Peacock M, Mosekilde L, Bouillon R, Lewiecki EM. Diagnosis of asymptomatic primary hyperparathyroidism: proceedings of the third international workshop. *J Clin Endocrinol Metab*. 2009 Feb; 94 (2):340-50. doi: 10.1210/jc.2008-1758.
19. Silverberg SJ, Lewiecki EM, Mosekilde L, Peacock M, Rubin MR. Presentation of asymptomatic primary hyper parathyroidism: proceedings of the third international workshop. *J Clin Endocrinol Metab* 2009; 94 (2): 351-65.

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20. Dawson-Hughes B, Harris SS, Dallal GE. Plasma calcidiol, season, and serum parathyroid hormone concentrations in healthy elderly men and women. *Am J Clin Nutr.* 1997 Jan; 65 (1):67-71.
21. Chapuy MC, Preziosi P, Maamer M, Arnaud S, Galan P, Hercberg S, Meunier PJ. Prevalence of vitamin D in sufficiency in an adult normal population. *Osteoporos Int.* 1997; 7 (5):439-43.
22. Adami S, Viapiana O, Gatti D, Idolazzi L, Rossini M. Relationship between serum parathyroid hormone, vitamin D sufficiency, age, and calcium intake. *Bone.* 2008 Feb; 42(2):267-70. Epub 2007 Oct 16.
23. Willett AM. Vitamin D status and its relationship with parathyroid hormone and bone mineral status in older adolescents. *Proc Nutr Soc.* 2005 May;64(2):193-203.
24. Elsammak MY, Al-Wosaibi AA, Al-Howeish A, Alsaeed J. Vitamin d deficiency in Saudi Arabs. *Horm Metab Res.* 2010 May;42(5):364-8. doi: 10.1055/s-0030-1248296. Epub 2010 Mar 8.
25. Arabi A, Baddoura R, El-Rassi R, El-Hajj Fuleihan G. Age but not gender modulates the relationship between PTH and vitamin D. *Bone.* 2010 Aug;47(2):408-12. doi: 10.1016/j.bone.2010.05.002. Epub 2010 May 7.
26. Ardawi MS, Sibiany AM, Bakhsh TM, Qari MH, Maimani AA. High prevalence of vitamin D deficiency among healthy Saudi Arabian men relationship to bone mineral density, parathyroid hormone, bone turnover markers, and lifestyle factors. *Osteoporos. Int.* 2012; 23(2):675-86.
27. Phelan PJ, O'Kelly P, Walshe JJ, Conlon PJ. The importance of serum albumin and phosphorous as predictors of mortality in ESRD patients. *Ren Fail.* 2008; 30(4):423-9. doi:10.1080/08860220801964236.

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