# HEALTHY LOOKIG HOSPITAL NURSES SHOWING VITAMIN D DEFICIENCY: CORRELATION OF VITAMIN D LEVELS WITH THEIR LEVELS OF PARATHHYROID HORMONE AND BONE TURNOVER MARKERS

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## ABSTRACT

***Objective:*** To evaluate the correlation of low vitamin D levels with parathyroid hormone (PTH) levels and bone turn over markers among apparently healthy hospital nurses.

***Methods:*** Screening was done on 50 recruited healthy female nursing staff, aged between 18 to 35 years, for vitamin D levels. Among them 31 were found to be deficient in vitamin D. These 31 nurses were selected for further evaluation in trance. Their vitamin D levels were calculated by using the electrochemiluminescence immunoassay. Blood samples were drawn to estimate serum PTH levels accordingly. Samples were also collected from these recruited subjects to evaluate their bone turn over markers, including, osteocalcin, procollagen type 1 N propeptide and Beta-Crosslaps.

***Results:*** Out of 50 subjects, 31 subjects were found to have Vitamin D levels below 50 nmol/l. Out of these 31 subjects, 13 subjects, 41.9%, showed vitamin D levels below 20 nmol/l. Among these 13 subjects, all had significantly raised PTH levels (*p*-value: <0.001, r-value: -0.781). In rest of all the subjects, including those having Vitamin D levels above 20nmol/l, inordinately, PTH levels were normal. No reciprocity was found between low Vitamin D and raised PTH levels with bone turnover markers, except with P1NP (r-value 0.022).

***Conclusion:*** PTH levels show a steep augmentation in serum, when vitamin D levels hit the trough below 20 nmol/l. These are the subjects who should be treated prior to the development of complications of bone resorption. Moreover we could not find any significant correlation of Vitamin D and PTH with any bone turnover marker except P1NP.

**Keywords:** Vitamin D deficiency, P1NP, Beta-Crosslaps, Parathyroid hormone**.**

## INTRODUCTION

Vitamin D is one of the most important component vital for bone health. Vitamin D deficiency causes impaired calcium absorption which can precipitate bone deformities including rickets and osteomalacia[1]. It is now a known fact that vitamin D deficiency is associated with osteoporosis and an increased risk for fractures[2].

Serum 25 Hydroxyvitamin D (25-OHD) is thought to be the most dependable indicator for vitamin D deficiency[3]. There are many causes of vitamin D deficiency. The World Health Organization construe the deficiency of vitamin D, by levels, dropped below 50 nmol/l[4].

Chief cells of the parathyroid glands secrete parathyroid hormone (PTH), also known as parathormone or parathyrin. PTH acts on the parathyroid hormone 1 receptor, which is present in highest amounts in bone and kidneys, to raise serum calcium levels in body[12].

Secondary hyperparathyroidism is caused by hypocalcemia, low calcium levels in blood, generates physiological (i.e. appropriate) secretion of parathyroid hormone (PTH) by the parathyroid glands. The most common cause of hypocalcemia is vitamin D deficiency. Vitamin D deficiency is caused by inadequacy of sunlight, diet or mal-absorption and chronic renal failure. Deficient vitamin D levels lead to hampered calcium absorption from intestine eventually producing hypocalcaemia and increased parathyroid hormone secretion. This increases

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bone resorption, in order to maintain the serum calcium.

Procollagen type 1 N propeptide (P1NP), can accurately identify those patients who are responding to anabolic or anti-resorptive therapy within 3 months of the start of treatment. The use of this biomarker in patients being treated for osteoporosis may significantly improve therapy adherence and clinical outcomes. Beta-Crosslaps (Beta-CTx) is released into the bloodstream during bone resorption and serves as a specific marker for the degradation of mature type I collagen. Elevated serum concentrations of Beta-CTx have been reported in patients with increased bone resorption.

We will observe the influence of low vitamin D levels on these bone markers; osteocalcin, P1NP, and Beta-CTx for assessment of bone formation and bone resorption.

Vitamin D levels below a certain point trigger the release of parathyroid hormone. One of the study from Iceland showed that vitamin D levels below 25 nmol/l significantly raised the parathyroid hormone leve[15]. So the critical question arises that at what level of vitamin D, parathyroid hormone significantly rises in our study group and does it cause significant bone resorption.

We carried out this study to understand the association between vitamin D and PTH and we then inspected the relationship between the two with the bone turnover markers.

## METHODOLOGY

Healthy females from nursing staff were randomly recruited in the study from January 2014 to June 2014. These subjects were being called for follow up in Rheumatology outpatient department.

We excluded those subjects who were taking any oral calcium supplement in the form of tablet or syrup in last 3 months, smokers, alcoholics, or those who have had major illness. Age, weight, height and age of menarche were registered. Baseline tests including blood complete picture, liver and renal functions tests were carried out. All the subjects had normal thyroid function tests. Only those subjects were recruited for the trance who have had these tests within normal range.

**Table: Correlation of Vitamin D levels with different variables (n = 31).**

| | Correlation r -value | *p*-value |
|---|---|---|
| Serum PTH level | - 0.781 | < 0.001 |
| Serum ALP level | 0.355 | 0.050 |
| Serum osteocalcin level | 0.217 | 0.242 |
| Serum P1NP level | 0.411 | 0.022 |
| Serum Beta-Crosslaps level | 0.127 | 0.497 |
| Serum calcium level | 0.143 | 0.443 |
| Serum phosphorus level | 0.201 | 0.279 |

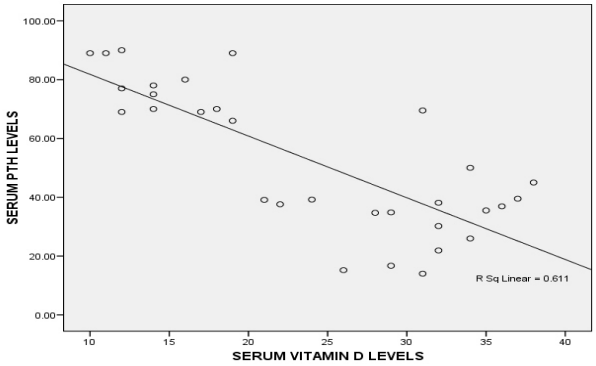


**Figure-1: Correlation of serum vitamin D level with serum PTH level (n = 31).**

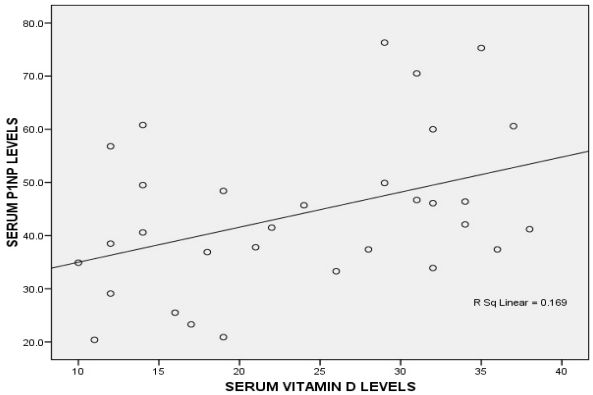


**Figure-2: Correlation of serum vitamin D level with serum P1NP level (n = 31).**

Fifty subjects from the nursing staff met the above criterion. Out of these, those who had low Vitamin D levels (< 50 nmol/l) were further enrolled in the study arm. Serum 25 Hydroxyvitamin D (25-OHD) levels were calculated using a chemi-luminescent immunoassay. Those patients with normal baseline tests and low vitamin D levels, had serum parathyroid hormone levels measured by two-site radioimmunoassay. Serum calcium, bone turnover markers including osteocalcin, P1NP, Beta-CTx levels were carried out in Fauji Foundation Hospital Rawalpindi laboratory.

Informed consent was taken from all the nursing staff and the study was being approved by the ethical committee of Fauji Foundation Hospital Rawalpindi.

## RESULTS

It was found that 31 nurses had low vit D levels. Average vitamin D level was 23.84 nmol/l (SD = 9.125, Range: 10 – 38 nmol/l). Thirteen (41.9%) nurses had vit D level less than 20 nmol/l. (For correlation of Vit D levels with different variables see table 1.) Average PTH level was 52.74 pg/ml (SD = 24.50, Range: 14 – 90). Serum vitamin D level had negative, strong and significant correlation with serum PTH level r = -0.781 ($p$ < 0.001). (Shown in fig-1). Average alkaline phosphatase (ALP) level was 185.32 IU/L (SD = 52.14, Range: 110 – 294). Average osteocalcin level was 29.83 ng/ml (SD = 9.98, Range: 12.5 – 49.64). Average P1NP level was 44.12 mcg/L (SD = 14.63, Range: 20.4 – 76.3). Average beta crosslaps level was 676.04 pg/ml (SD = 381.76, Range: 105.7 - 1502). Average calcium level was 2.174 mmol/l (SD = 0.096, Range: 2 – 2.47). Average phosphorus level was 1.224 mmol/L (SD = 0.118, Range: 1 – 1.41). Vit D levels had positive, moderate and significant correlation with P1NP level r = 0.411 ($p$ = 0.022). (Fig-2) Correlation with serum ALP level was positive and moderate but it had borderline significance i.e. r = 0.355 ($p$ = 0.050).

## DISCUSSION

In our study we found 62% of the subjects had low vitamin D levels as defined by the WHO criterion[4]. Multiple studies have been done, showing vitamin D deficiency from 35-55% in population. One of the study from USA showed an overall prevalence rate of vitamin D deficiency of 41.6%[8].

In our study we found an inverse relationship between vitamin D levels and PTH levels. Those patients in which the vitamin D level fell below 20 nmol/l, their PTH level also started to rise significantly. One of the studies from Iceland revealed that vitamin D levels below 25 nmol/l were associated with significantly raised PTH levels[5]. Similarly studies have been done showing that those patients who have a rising vitamin D levels, with calcium and vitamin D supplements their PTH falls significantly[8]. So it means that one should treat only those patients who have vitamin D level below 20 nmol as this is the point where bone resorption starts, well it is still an unanswerable question as till now the recommendations are controversial[9]. One of the study from Australia has shown that levels of vitamin D significantly rise in post-menopausal women who were taking vitamin D more than 1000 IU and calcium intake above 800 mg/day[6].

There is a strong correlation of low vitamin D with bone turn over markers in various studies, however we could not find any statistically significant correlation, except with P1NP. These results were quite close to one of the study showing no differences in bone turnover markers in patients with low 25-OHD[10], while some studies show that there is significant increase in the bone turnover markers with low vitamin D levels[11].

There are many limitations of the study including the small study group, this could be one of the reasons of not finding any significant relationship with the bone turnover markers. We failed to find out any threshold value of vitamin

D at which PTH plateaus. Moreover no correlation of low vitamin D and raised PTH was seen with the bone density.

We conclude that there is a significant deficiency of vitamin D in healthy individuals. In our study we found 62% of the subjects had low vitamin D levels. We also found that levels of vitamin D below 20 nmol/l leads to secondary hyperparathyroidism. However we could not find any correlation of this secondary hyperparathyroidism and low vitamin D level with the bone turn over markers, except P1NP in our study.

## Conflict of Interest

This study has no conflict of interest to declare by any author.

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