

Serum Vitamin D in Common Non-Metabolic Disorders: Results of Patients' Survey at Public Hospitals of Karachi

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ABSTRACT

Objectives: To determine serum vitamin D level in common non-metabolic medical and surgical disorders.

Study design: Cross sectional study.

Place and duration of study: Study conducted from March 2006 to January 2009 at multiple centres as per author's affiliation.

Patients and methods: Patients having a common non metabolic symptomatic disease were selected. Patients with rickets and osteomalacia were excluded. Serum vitamin D, serum calcium, phosphorus, alkaline phosphatase level and routine blood investigations were obtained in all patients. Normal range of serum vitamin D level was defined and lower values were divided into mild, moderate and severe. One sample t test was used for determination of significance. All data were collected and processed on SPSS version 10.

Results: Out of 205 patients, serum vitamin D level was found to be low in 169 (82.4%) patients. The vitamin D level was normal in 36 (17.6%) patients; low levels were categorized into three, mildly low in 33 (16.1%) patients, moderately low in 55 (26.8%) patients and severely low in 81 (39.5%) patients. Chi square test and one sample test (P value = < 0.001) with all type of deficiencies in all groups of diseases was highly significant.

Conclusion: Low serum vitamin D level with highly significant value seen in all groups of diseases and in all types of deficiencies. Its prognostic value, role in the development of the pathology and pathogenesis in different diseases has to be evaluated, and require further research in individual sets of diseases.

Key words: Vitamin D, calcium metabolism, alpha calcidol.

INTRODUCTION

During the past decade, important advances in the study of vitamin D had been made. In addition to its important role in skeletal development and

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Received: January 30, 2009; accepted: November 11, 2009

maintenance, evidences suggests that vitamin D produces beneficial effects on extra-skeletal tissues and that the amounts needed for optimal health were probably higher than previously thought. At the same time, numerous reports¹⁻³ have shown that relatively high proportions of people have inadequate levels of vitamin D. The extra skeletal health benefits of vitamin D and high prevalence of inadequate levels

of vitamin D have been largely unrecognized by both physicians and patients.

Vitamin D is one of the misnomer biochemical agent. Fundamentally its active component is 1alpha, 25-dihydroxyvitamin D, which is a hormone. It is indispensable for health. Chemically it is a steroid hormone, like estrogen, progesterone, testosterone and cortisol. It works through the specific receptors called VDRs (vitamin D receptors).³ VDRs are present in nearly every tissue of body including bones and soft tissues. So deficiency of this vitamin can involve roughly any tissue in every disease process.⁴ VDRs are proteins in nature and present on the surface of the nuclear membrane. Vitamin D enters the target cell and interacts with its nuclear VDRs, causing augmentation or depression of transcription of vitamin D-responsive genes in the respective tissue cells.⁵ Thus the effects of vitamin D are wide spread and long lasting.

The recommended dosage of vitamin D for different age group is 200 IU in most of the patients. However in old age and in pregnancy, the requirement is increased to 400 - 600 IU.⁶ Though, in older patients with osteoporosis, for the prevention of fracture, the estimated blood level of vitamin D should be 70-80nmol/l. That can be achieved by a dose of 20-25µg/day or 800-1000 IU,⁷ especially in women and old age men. This roughly doubles the suggested dose of WHO.⁷ Similarly the required dose of vitamin D has to be increased, if sunlight exposure is limited.⁸

There is a growing evidence that deficiency of vitamin D is involved in many diseases.⁹⁻¹⁰ Inadequate levels of vitamin D are very common in old age.¹¹ In a European based study, serum level of vitamin D in patients, not taking supplements was, 19.3 ng/ml with standard deviation of 11.0. In patients taking

supplements it was 21.6 ng/ml with standard deviation of 8.7.¹¹

There is a distinct relationship between fracture healing and vitamin D. Virtually all patients hospitalized for fracture have vitamin D inadequacy.¹² In experimental study on animals, the plasma concentration of vitamin D rapidly decreased on day 3 and continued to decrease up to 10 days, after fracture. This rapid disappearance of 1, 25(OH) vitamin D3 in the early stages after fracture was not due to either increased degradation or decreased synthesis of 1, 25(OH) vitamin D3, but rather to increased utilization. This was confirmed by radioactive labeled vitamin D, as it was concentrated in the callus.¹³ In another human study, comparative decrease in 24, 25(OH) vitamin D3 values was also noted in all patients. These changes reflect the consumption of these metabolites during healing at the fracture site.¹⁴ No data is available of local population, for Vitamin D levels in diseases except the observational study of author¹⁵ which showed deficiency of vitamin D upto 92% in non metabolic conditions. This study was conducted, to have a base line idea in general randomly selected patients. The objective of this study was to determine serum vitamin D level in common non-metabolic medical and surgical conditions.

PATIENTS AND METHODS

This cross sectional hospital based study was conducted from March 2006 to January 2009. Data for surgical conditions were collected of out patients as well as in patients from orthopedic and surgical units of Civil Hospital and Lyari General Hospital Karachi. Data for non-surgical conditions were collected from Medical OPD and ward of Abbasi

Shaheed Hospital Karachi. Surgical patients were defined as those requiring surgery as a definitive remedial measure. While non surgical patients were those in which no surgical procedure was required, however they were diagnosed to have an organic disease requiring medical therapy. Patients selected for elective or emergency surgery for one or other reason was grouped as pre surgical patients, they were 30 in number. In this group two samples of blood were taken, one before surgery and the other 48 hours after surgery. Every 5th patient was selected with organic disease supported by signs & symptoms and laboratory confirmation. Patients who were taking vitamin D in any form since last 3 months, or had chronic renal disease & taking steroids (corticosteroids or sex steroids anabolic steroids) in any form and those with rickets & osteomalacia were excluded from study. Verbal consent of the selected patients were obtained. Serum vitamin D levels of all patients were obtained alongwith serum calcium, phosphorus, alkaline phosphatase and routine blood investigations. For collection of serum calcium, blood samples were collected without application of tourniquet. The normal range of serum vitamin D was taken 31-100 ng/ml, 21-30 ng/ml as mildly low, 10-20 ng/ml as moderately low, and levels below 10ng/ml were labeled as severe deficiency.¹⁶ Data was collected and processed on SPSS version 10. Results were described as percentages. One-sample t-test and Chi- square were used to determine the significance, which was taken as $p < 0.05$.

RESULTS

A total of 205 patients were included in this study. Out of those 126 (61.5%) were females and 79 (38.5%) were males. The mean age of patients was 42.8 ± 16.3 years. (R: 2-80)

Table 1: Age distribution

Age group	Female	Male	Total
1-10	1 (0.4%)	2 (0.9%)	3 (1.4%)
11-20	10 (4.8%)	4 (1.9%)	14 (6.8%)
21-30	28 (13.6%)	13 (6.3%)	41(20.0%)
31-40	23 (11.2%)	16 (7.8%)	39 (19.0%)
41-50	23 (11.2%)	18 (8.7%)	41 (20.0%)
51-60	23 (11.2%)	16 (7.8%)	39 (19.0%)
61-70	10 (4.8%)	8 (3.9%)	18 (8.7%)
over 70	8 (3.9%)	2 (0.9%)	10 (4.8%)
Total	126 (61.5%)	79 (38.5%)	205 (100%)

Majority of patients were house wives and with good socio economical status and only 25.0% belonged to poor socio economical group. Socio economical grouping were made according to their monthly income.

Table 2: Frequency of distribution for occupation of the studied group

Occupation	Female	Male	Total
Banker/ accountant / Businessman	2 (0.9%)	5 (2.4%)	7 (3.4%)
School teacher/Clerk	1 (0.4%)	7 (3.4%)	8 (3.90%)
Doctor	2 (0.9%)	5 (2.4%)	6 (2.9%)
Domestic servant/ cook/ driver	2 (0.9%)	7 (3.4%)	9 (4.3%)
Engineer	0	3 (1.4%)	3 (1.4%)
Govt officer/ Executive officer	0	5 (2.4%)	5 (2.4%)
Non working ladies.	108 (52.6%)	0	108 (52.6%)
Industrial worker/farmer	1 (0.4%)	11(5.3%)	12 (5.8%)
Retired	1 (0.4%)	14 (6.8%)	15 (7.3%)
Sales girl/man	1 (0.4%)	12 (5.8%)	13 (6.3%)
Student	7 (3.4%)	6 (2.9%)	13 (6.3%)
Paramedic	1 (0.4%)	4 (1.9%)	5 (2.4%)
Total	126 (61.5%)	79 (38.5%)	205 (100%)

Serum vitamin D levels were done in 205 patients. Low levels were found in 169(82.4%) patients, with a mean of 17.2 ± 13.81 . Vitamin D level was normal

in 36 (17.6%) patients. It was mildly low in 33 (16.1%) patients, moderately low in 55 (26.8%) patients and severely low in 81(39.5%) patients. The deficiency was highly significant in patients with diabetes, infection and pre surgical conditions (P<0.001) and it was significant in other four groups of diseases (P<0.05) as seen in table 3.

Table 3: Vitamin D deficiency/normal with respect to diagnosis.

Diagnosis	Vitamin D deficient	Normal vitamin D	Value of Significance	Total/percentage
Diabetes	24 (11.7%)	5 (2.4%)	0.001	29 (14.1%)
Infections	40 (19.5%)	5 (2.4%)	0.001	45(21.9%)
Muscular weakness	25 (12.1%)	9 (4.3%)	0.006	34(16.5%)
Osteoporosis	26 (12.6%)	8 (3.9%)	0.002	34(16.5%)
Obstructive. Lung diseases/Allergic sinusitis	13 (6.3%)	2 (0.9%)	0.005	15(7.3%)
Pre surgical patients	27(13.1%)	3 (1.4%)	0.001	30(14.6%)
Rheumatoid arthritis	14 (6.8%)	4 (1.9%)	0.012	18(8.7%)

Amongst infections 03 patients had chronic osteomyelitis of tibia,02 patients had hepatitis C, 01 patient had hepatitis A, 01 patient had resolving pneumonia, 03 patients had septic arthritis of hip and 34 patients had tuberculosis. In tuberculosis, 17 patients had intestinal tuberculosis, 14 patients had pulmonary tuberculosis, 03 patients had spinal tuberculosis and 01 patient had tuberculous meningitis. Serum calcium and vitamin D were low in all patients with tuberculosis. However, both the serum phosphorus and alkaline phosphatase levels did not show any relation with type and severity of vitamin D deficiency in tuberculosis. Where as serum calcium, phosphorus and alkaline phosphatase were disturbed in other diseases. Serum calcium was low in 80 (39.0%) patients and normal in 125 (61.0%) patients. Serum phosphorus level was low in 10 (4.9%) patients, normal in 183 (89.3%), and raised in 12 (5.9%). Serum alkaline phosphatase was low

in 1 (0.5%), raised in 18(8.8%) and normal in 186 (90.7%) patients.

Table 4: Frequencies with percentage of vitamin D deficiencies in different groups.

Diagnosis	Normal vitamin D Level		Low vitamin D Level	
	Male	Female	Male	Female
Diabetes	4 (1.9%)	1 (0.4%)	11 (5.3%)	13 (6.3%)
Infections	3 (1.4%)	2 (0.9%)	11 (5.3%)	29 (14.1%)
Muscular weakness	3 (1.4%)	6 (2.9%)	12 (5.8%)	13 (6.3%)
Osteoporosis	0	8 (3.9%)	4 (1.9%)	22 (10.7%)
Obs. Lung diseases /Allergic sinusitis	1 (0.4%)	1(0.4%)	5 (2.4%)	8 (3.9%)
Pre surgical patients	3 (1.4%)	0	18(2.4%)	9 (4.3%)
Rheumatoid arthritis	1 (0.4%)	3 (1.4%)	3 (1.4%)	11 (5.3%)
Total	15(7.3%)	21(10.2%)	64 (31.2%)	105(51.2%)

DISCUSSION

Deficiency of vitamin D is a worldwide problem.¹⁷ About 59% of world population is suffering from this vitamin deficiency.¹⁷ In America minimum deficiency has been seen in Latin America (51%). Where as Europe (52%) Australia (59%) and Asia (63%) are in middle zone. The most severe deficiency is seen in the Middle East (82%).¹⁷ Deficiency in this part of the world is found to be around 82.4 %, slightly higher than Middle East due to the factors of urbanization and social reasons, including less exposure to sun, mostly seen amongst females. In addition, majority of our dietary products are not fortified with vitamin D. Another reason for vitamin D deficiency, seen world over is the smaller dose of only 400 IU of vitamin D, which was previously recommended. Recent study by Heaney, *et al*¹⁸ conclude that healthy men utilize between 3,000–5,000 IU of cholecalciferol a day. This intake is enough to maintain the blood level of vitamin D between 30-50 ng/ml.¹⁸⁻¹⁹

This study showed significant deficiencies with lowest value of vitamin D, irrespective of concomitant diseases included in the study, which correlates with

the finding of Holick,¹⁶ in a recent article Fair amount of research has shown that vitamin D deficiency plays a role in the development of Diabetes.²⁰ This study also showed that 24 (11.7%) patients with diabetes had deficiency of vitamin D. It has also been observed that correction of serum level of vitamin D makes the diabetic control easier to achieve. This is probably due to the fact that absence of adequate levels of vitamin D causes impaired release of insulin.²⁰⁻²¹

Chronic infection like tuberculosis is also known to be associated with low serum vitamin D.²²⁻²³ In this study almost all tuberculous patients showed highly significant deficiency which is in agreement with Sasidharan et al and Wilkinson et al.²²⁻²³ Patients with soft tissue rheumatism, a fibromylgia syndrome, are often misdiagnosed as chronic fatigue syndrome. Low levels of vitamin D has been demonstrated in patients with fibromyalgia.²⁴⁻²⁵

This study showed 34 (16.5%) cases of muscular weakness and 18(8.7%) of soft tissue rheumatism, who had significant vitamin D deficiency.

Table 5: Significant values of vitamin D in various diseases

Diagnosis	Testing value 30
Diabetes	<.001
Infections	<.001
Muscular weakness	.001
Osteoporosis	.005
Obstructive Lung diseases/Allergic sinusitis	.001
Pre surgical patients	<.001
Rheumatoid arthritis	.001
Types of deficiencies were:	
Mild deficiency	<.001
Moderate deficiency.	<.001
Severe deficiency.	<.001

Osteoporosis is a common disorder of this part of world.¹⁵ In this study 34(16.5%) showed highly significant deficient level. This finding was also matching with findings of our contemporaries abroad.⁷⁻⁸

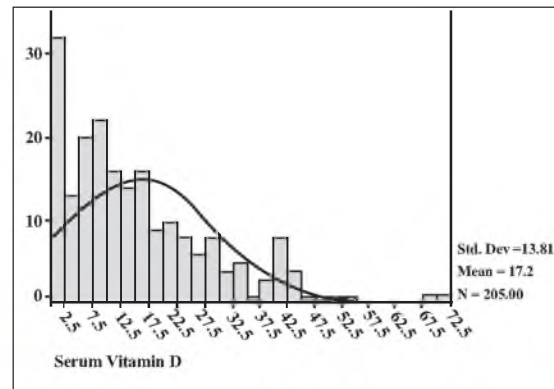


Figure – 1 : Histogram of vitamin D deficiency

Two samples of blood were taken from 30(14.6%) patients of pre surgical group, one before surgery and one after 48 hours of surgery. They also showed low serum vitamin D levels with highly significant P value with one sample T test and Chi Square test for both samples. In addition the difference between the means of two samples were (pre and postoperative) also significant(P value= .003), when paired T test was performed, indicating a significant drop in serum vitamin D after surgical stress. In literature, we were able to find that surgical stress can cause significant drop in vitamin D.²⁶⁻²⁷

In this study however serum level of all rheumatoid patients shows mild to severe deficiency. P value for t test was highly significant and Chi Square test was (0.012) significant in our study. Data from other studies also indicated that, the role of vitamin D is also important for prevention of some autoimmune diseases like multiple sclerosis, lupus, and rheumatoid arthritis.²⁸

CONCLUSIONS

Low serum vitamin D levels with highly significant values is seen in all groups of diseases and in all types of deficiencies. Its prognostic value, role in the development of the pathology and pathogenesis in different diseases has to be evaluated, and require

further research in individual sets of diseases.

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