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# Evaluating the Frequency of Vitamin D Deficiency in the Pediatric Age Group and Identifying the Biochemical Predictors Associated with Vitamin D Deficiency

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## Abstract

**Objective:** To determine the frequency of Vitamin D deficiency in the Peadritic population Pakistan.

To identify the biochemical predictors associated with Vitamin D deficiency.

**Method:** A cross sectional study was conducted in an urban tertiary care hospital, on, infants and children up to the age of 15 years who were seen in inpatient and in the outpatient department. Serum Vitamin D levels were measured along with a biochemical profile which included Serum Calcium, Serum Phosphate, Serum Alkaline Phosphate and Serum Parathyroid Hormone. The results were then analyzed using SPSS 20.

**Results:** Out of the 293 samples included in the study, frequency of children with Vitamin D deficiency was found out to be 77% (n = 227 ). 48% (N = 142) of the total sample had severe deficiency although showed no clinical signs of Rickets. Patients with Vitamin D deficiencies were also found out to have secondary hyperparathyroidism and hypophosphatemia although serum calcium levels were normal.

**Conclusion:** Through our study we found out that Majority of the children coming to Ziauddin were deficient in Serum Vitamin D. We suggest that adequate supplementation of Vitamin D should be started from an early age to prevent clinical effects of the deficiency in the long term.

**Keywords:** Vitamin D deficiency; Prevalence; Serum calcium; Serum phosphate; Serum parathyroid hormone

## Abbreviations

Vitamin D: 25-Hydroxycholecalciferol; OPD: Out Patient Department; PTH: Parathyroid Hormone

## Background

Vitamin D is a fat-soluble prohormone, responsible for the absorption of calcium from the gut [1]. Egg yolks, seafood oil, beef liver, and oily seafood are considered the best sources of Vitamin D [1]. Moreover, most of the Vitamin D utilized by the human body is primarily made in the skin when it is exposed to Ultraviolet radiation [1].

It is estimated that the current prevalence of vitamin D in children is between 30% to 80% [2,3]. Currently, it is considered that although a vast majority of children living in Asian Countries have some degree of Vitamin D deficiency, only a very small proportion of these patients present with symptoms of the rickets.

Local data available on the prevalence of Vitamin D deficiency on Pakistani children is scarce. In a study conducted in England, it showed that 34% (n = 200) of Pakistani children residing in UK had some form of Vitamin D deficiency [4]. Furthermore, Pakistani children were found out to be the most deficient in serum Vitamin D concentrations compared to the rest of the sub-continent [4].

In the current study we sought to determine the frequency of Vitamin D deficiency in infants and children from 0-15 years of age coming to a tertiary care setup in an urban setting.

The primary objective was to test weather Vitamin D deficiency (serum 25-hydroxycholecalciferol concentrations <20 ng/ml) is prevalent among healthy infants and children. The secondary objective was to see the relationship of Vitamin D levels with Parathyroid Hormone levels, Serum Calcium levels, Serum Phosphorus levels and Serum Alkaline Phosphate Levels.

## Definitions

The children were divided into three diagnostic categories according to Serum 25-Hydroxycholecalciferol levels (Table 1).

| | |
|---|---|
| Normal | Greater than 30 ng/ml |
| Moderate Deficiency | 20-30 ng/ml |
| Severe Deficiency | Less than 20 ng/ml |

**Table 1:** Vitamin D deficiency range.

The definition of Vitamin D deficiency was based on reference from expert consensus that a Serum 25-Hydroxycholecalciferol level of 20

ng/ml or less is the appropriate diagnostic threshold for deficiency [5,6]. Serum25-Hydroxycholecalciferol level has been shown to be inversely coorelated with PTH level at concentrations of 30-40 ng/ml [7] and health experts agree that 30 ng/ml represent an optimal level of 25-Hydroxycholecalciferol .

## Method

This study was conducted at Ziauddin Medical University, Nazimabad Campus. The Peadritic department provides tertiary care facilities for approximately 6000 children annually, which live within the adjacent urban community of upper, middle and lower class.

The sample size of the study was calculated using the prevalence of Vitamin D deficiency in children [2,3]. As there were varying figures of prevalence the final prevalence was taken to be the highest reported which was 80%. An additional 15% of samples were added to exclude non-response and poorly-filled questionnaires. The margin of error was taken at 5% with 95% confidence level. A total of 293 samples were then included in the study.

Children aged between 0-15 years were taken into the study. Children admitted to the Peadritic ward and those who came to the Outpatient clinic with problems other than Vitamin D deficiency were taken into the study. The children were selected through convenience sampling. Parents or guardians provided informed written consent at time of study enrollment. The hospital ethical committee approved the protocol.

Data was collected at the time of admission/inclusion in the study which included age, sex, weight and nutritional history. A thorough physical examination was conducted to exclude any signs of Rickets.

Children coming to the OPD or admitted to the ward with problems other than known vitamin D deficiency and showed no signs of Vitamin D deficiency were included in the study. Children who had known Vitamin D deficiency, or were suffering from Parathyroid Hormone Disorders or with Metabolic Bone Diseases were excluded from the study. Also Children with Chronic Diseases or who had taken medications known to affect Vitamin D metabolism in the last six months were also excluded.

One blood sample of 5ml was obtained from each child. Blood tests were performed in the hospital laboratory. Serum 25-Hydroxycholecalciferol levels were determined by using a chemiluminesence assay. Serum Calcium, Phosphorus and alkaline phosphate were measured using an end point assay in a multi-channel analyzer. Intact PTH was measured using a 2-site chemiluminesence immunoassay. Samples were analyzed in multiple assays.

We took out frequency of Vitamin D deficiency in our target population. We used Pearson Chi-square test to compare the association of Vitamin D deficiency between infants and children and the demographic variables such as age and gender.

To identify relationship between biochemical predictors and Vitamin D. We categorized each patient in having a deficiency, excess or normal values of Serum Phosphate, Serum Calcium, Serum Alkaline Phosphate and Serum Parathyroid Hormone. We used Pearson Chi-square test to determine the association between Serum Vitamin D and the biochemical predictors, if present.

The study was funded by the patients themselves, after consent was taken from them. They were explained the procedure completely before consent was taken.

## Results

The sample included 293 infants and children, out of which 142 (48%) children found to have severe Vitamin D deficiency (Figure 1).

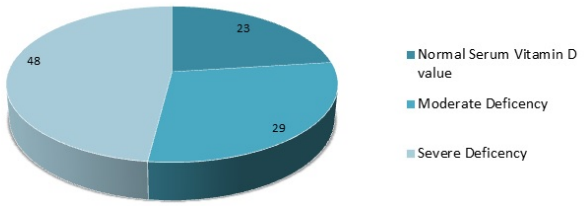


**Figure 1:** Severity of vitamin D deficiency.

| Vitamin D Deficiency | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | Normal (n = 66) | | Moderate Deficiency (n = 85) | | Severe Deficiency (n = 142) | | P- Value |
| | | n | n | % | n | % | N | % | |
| **Gender** | Male | 159 | 33 | 20.8% | 51 | 32.1% | 75 | 47.2% | 0.421 |
| | Female | 134 | 33 | 24.6% | 34 | 25.4% | 67 | 50% | |
| **Age** | Neonatal (upto 1 month) | 30 | 4 | 13.3% | 20 | 66.7% | 6 | 20% | 0.000 |
| | Age 1 month to 1 year | 54 | 13 | 24.1% | 10 | 18.5% | 31 | 57.4% | |
| | Age 1 year to five years | 89 | 28 | 31.5% | 25 | 28.1% | 36 | 40.4% | |
| | Age 5 years to 15 years | 120 | 21 | 17.5% | 30 | 25% | 69 | 57.5% | |

**Table 2:** Vitamin D deficiency and its relation to demographic variables.

We compared the demographic variables of our sample in terms of age and gender. Although, there was no statistical difference between gender predisposition and Vitamin D deficiency, P-value was statistically significant for different age groups (p-value = 0.00) (Table 2).

The results showed that in the neonatal age group 66.7% (n = 20) patients had moderate Vitamin D deficiency. This was the highest when we compared it to other age groups. 57.4% (n = 31) of the patients in the 1 month to 1 year age group showed severe Vitamin D deficiency. Similarly, 57.5% (n = 69) of the patients in the school going age group (5-15 years) showed severe Vitamin D deficiency.

Among the biochemical markers which included Serum Calcium, Serum Phosphate, Serum Alkaline Phosphate and Serum Parathyroid Hormone, only Serum Phosphate showed statistically significant relationship (p-value = 0.000) with Vitamin D levels (Table 3).

| Vitamin D Deficiency | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | Normal (n = 66) | | Moderate Deficiency (n = 85) | | Severe Deficiency (n = 142) | | P- Value |
| | | n | n | % | n | % | N | % | |
| **Serum Calcium** | Decreased Serum Calcium Levels | 14 | 3 | 4.5 | 5 | 5.9 | 6 | 4.3 | 0.847 |
| | Normal Serum Calcium Levels | 278 | 63 | 95.5 | 80 | 94.1 | 135 | 95.7 | |
| **Serum Phosphate** | Decreased Serum Phosphate Levels | 81 | 5 | 7.9 | 13 | 15.5 | 63 | 47.7 | 0.000 |
| | Normal Serum Phosphate Levels | 135 | 37 | 58.7 | 50 | 59.5 | 48 | 36.4 | |
| | Increased Serum Phosphate Levels | 63 | 21 | 33.3 | 21 | 25 | 21 | 15.9 | |
| **Serum Alkaline Phosphate** | Normal Alkaline Phosphate Levels | 240 | 54 | 88.5 | 76 | 92.7 | 110 | 85.3 | 0.263 |
| | Increased Alkaline Phosphate Levels | 32 | 7 | 11.5 | 6 | 7.3 | 19 | 14.7 | |
| **Serum Parathyroid Hormone** | Decreased Serum Parathyroid Hormone Levels | 8 | 1 | 2.6 | 4 | 6 | 3 | 3.2 | 0.064 |
| | Normal Serum Parathyroid Hormone Levels | 110 | 27 | 69.2 | 33 | 49.3 | 50 | 53.8 | |
| | Increased Serum Parathyroid Hormone Levels | 81 | 11 | 28.2 | 30 | 44.8 | 40 | 43 | |

**Table 3:** Vitamin D deficiency and its association with biochemical markers.

Calcium levels in 95% (n = 278) of our patients was found out to be normal. In the patients with normal Serum Calcium values, 48.6% (n = 135) of the patients showed severe Vitamin D deficieny, 28.8% (n = 80) showed moderate deficiency whereas only 27.4% (n = 37) had normal Vitamin D values. We also saw that there was no statistically significant relationship between Serum Calcium and Serum Vitamin D levels. It seems that there may be a bias in the assessment of ages and their consequent implications on the levels.

The results showed that there was a a statistically significant (p-value = 0.00) relationship between Serum Phosphate and Serum Vitamin D levels in our study. It was seen that out of 81 patients that showed decreased levels of Serum Phosphate, 77.8% (n = 63) also showed severe Vitamin D deficiency. Only 5 patients that had decreased phosphate levels had normal Vitamin D values. This relationship clearly showed that there was an association between hypophosphatemia and Vitamin D deficiency.

Serum Parathyroid hormone level being a more expensive test, could not be afforded by 94 (32%) of the patients included in the study. Thus, this data was not reported.

## Frequency of Vitamin D Deficiency

77% (n = 227) of the patients coming to the OPD were found to be deficient in Vitamin D. Out of the 227 patients that had Vitamin D deficiency, 63% (n = 142) had severe Vitamin D deficiency. Only 23% of the sample had Vitamin D levels at the optimal threshold.

## Discussion

Vitamin D levels in children and infants living in an urban setting of Karachi were found to be significantly lower than the optimal threshold. Interestingly, although majority of our sample had Vitamin D deficiency none of them showed any signs of Rickets on physical Examination.

According to Absoud [7], in a study published in the United Kingdom in 2011, Serum Vitamin D levels were found to be deficient in both sexes and there was no difference in magnitude of deficiency between boys and girls. Similarly, in our study we found out that equal proportions of male and female children were severely deficient in

serum Vitamin D concentrations. The results showed that there was no association between Serum Vitamin D concentrations and Gender distribution.

Majority of the neonates which were included in our study had Vitamin D deficiency. This could be related to the decreased Vitamin D levels in mothers which will cause decreased stores in the newborn. Multiple studies conducted in Pakistan [8,9] and in other parts of the world [10-15] which have discussed that there is a severe deficiency of Vitamin D in Mothers which have resulted in their newborns developing the deficiency. This again presses on the importance of proper Calcium and Vitamin D supplementation of mothers during pregnancy. A study conducted in Iran [16], proved that mothers who had been given proper nutritional supplementation during pregnancy, their offspring had higher cord blood Vitamin D levels compared to neonates whose mothers weren't supplemented properly.

In our study, we found out that a high proportion of Children going to school also had Vitamin D deficiency. Pakistan being a sub-tropical country is sun-rich. Despite the sun exposure, we found out that 84% of the children going to school had some form of Vitamin D deficiency. These findings were consistent with studies in countries such as Iran [17], Lebanon [18], Israel [19], Saudi Arabia [20] and Qatar [21] where although there is adequate sun exposure school going children were found to have Vitamin D deficiency.

Despite the fact that most of the children included in our study had Severe Vitamin D Deficiency, majority had normal levels of Calcium but Serum phosphate was low in these children. Apart from this most of the children had normal levels of Serum Alkaline Phosphate but an increased serum parathyroid level. Studies conducted in Europe [22,23] correlate a negative relationship between Serum Vitamin D levels and Serum Parathyroid levels. These studies were conducted on Elderly population who showed secondary hyperparathyroidism along with Vitamin D deficiency. After proper Vitamin Supplementation of these individuals, PTH levels were shown to come back to normal. Our results could also be explained by the fact that low levels of Vitamin D could have caused an increase in PTH levels.

Secondary hyperparathyroidism is known to cause excessive Phosphate excretion from the kidneys. This explains why majority of our patients had low levels of serum phosphate although circulating levels of Calcium and Alkaline Phosphate was completely normal. Normally in the third world countries Serum Calcium, Phosphate and Alkaline Phosphate are routinely studied. Serum Vitamin D is not readily done as it is not easily available and is also an expensive modality. We suggest that any child presenting with hypophosphatemia should be also investigated for Vitamin D deficiency along with other causes in the Peadritic population.

Through our study we saw that there was a severe deficiency of Vitamin D in the Peadritic population coming to the hospital. Due to this children are at a very high risk of developing Rickets. Apart from this, Vitamin D deficiency has also been known to increase the risk of Asthma [24] and Type 1 Diabetes [25] amongst other diseases. A study conducted in India [26] proves that Subclinical Vitamin D deficiency is also a strong risk factor for developing Acute Lower respiratory tract infections in children under five years. Similarly, low levels of Vitamin D have also been associated with Respiratory Syncytial Virus Bronchiolitis in otherwise healthy neonates [27]. A Study conducted in Turkey [28] suggested that proper supplementation of Vitamin D should be started immediately after birth and should continue well beyond first year of life to prevent Vitamin D deficiency.

The major limitation in the study was that as this study was funded by the patients themselves, who had agreed after signing the consent form. These tests being expensive, a few of the patients could not afford the complete biochemical panel and thus we had missing data. Regardless, all of the patients who showed serodeficiency of Vitamin D were prescribed Vitamin D supplementation.

## Conclusion

Although, Vitamin D deficiency is very common in Pakistan there is no any protocol for proper supplementation to children. The International Peadritic Association recommends that infants and children aged 0-1 years require at least 400 IU/d of Vitamin D and children 1 year and older require 600 IU/d of Vitamin D to maximize bone health. Similarly, we suggest that Pakistani Children should also be given Vitamin D supplementation from an early age to prevent the deficiency which could lead to various short and long term health problems.

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