ASSESSMENT OF VITAMIN D AND CALCIUM LEVELS IN MULTI TRANSFUSED β-THALASSEMIA SYNDROME PATIENTS OF DISTRICT PESHAWAR

Tariq Hamayun1, Nazish Farooq*, Tariq Masood1

ABSTRACT

Background: Thalassemia syndrome represents a heterogeneous group of inherited anemias. It is one of the most common hereditary genetic disorders in Pakistan. Vita-min D is an important metabolite known to be deranged in various systemic illnesses involving kidneys, liver, GIT and endocrine system. Defective synthesis of 25-OH vitamin D have been described in these patients which negatively affect their bone metabolism. Impaired calcium homeostasis is thought to be a consequence of iron overload seen in multi-transfused thalassemia patients. Objective of the study was to assess serum vitamin D and calcium levels in B thalassemia syndrome patients of district Peshawar.

Methodology: The current study had descriptive study design with cross-sectional time prospect. A total of 141 thalassemia syndrome patients were enrolled in the study. Physical examination was performed followed by collection of blood samples. The samples were then processed and analyzed in the laboratories of Institute of Basic Medical Sciences, Khyber Medical University, Peshawar.

Results: The mean age of our study group patients was 12.62±5.10 years. The mean 25-OH Vit D levels were 17.48±11.34 ng/dl, while mean total serum Ca concentration was 8.67±9.1 mg/dl. Only 21.3% of our patients had optimal/normal levels of serum vitamin D concentration. 72.3% of our study patients had normal levels of their total serum calcium, while 27% of patients had low total serum calcium levels and 0.7% had high levels for serum calcium.

Conclusion: The present study showed a high prevalence of VDD and low total serum calcium levels in thalassemia patients with a significant low BMI, that signify the importance of screening for said metabolites and appropriate therapeutic interventions. The presence of such metabolic derangements may be due to the presence of high serum ferritin levels and poor nutrition intake.

Appropriate measurements therefore should be taken to improve health and quality of life in thalassemia patients.

Keywords: Thalassemia syndrome, 25-OH Vitamin D, Calcium, Body mass index (BMI)

INTRODUCTION

Thalassemia syndrome represents a heterogeneous group of inherited anemias signified by defective synthesis of one or more globin chain subunits of haemoglobin (Hb) tetramer. Thalassemia are autosomal recessive disorders. There are several types of thalassemia with clinical picture ranging from barely detectable hematological abnormality to severe and fatal anemia. The defect primarily is quantitative i.e. reduced or absent synthesis of the normal globin chains, but there are mutations as well which result in structural variants produced at reduced rate (e.g. HbE, Hb Lepore). This results in reduced hemoglobin in red blood cells (RBCs) as well as decreased production of RBCs that consequently leads to anemia.
Vitamin D is essential for calcium homeostasis and for mineralization of skeleton, especially during periods of rapid growth like infantile and pubertal growth periods. Vitamin D deficiency (VDD) can lead to rickets (a mineralization defect at the epiphyseal growth plates and bone tissue) and osteomalacia (a mineralization defect of bone tissue). In thalassemia patients, bone disease becomes an important cause of morbidity that includes rickets, osteoporosis, spinal deformities, scoliosis, fractures and nerve compression.

Vitamin D is an important metabolite known to be deranged in various systemic illnesses involving kidneys, liver, gastrointestinal tract (GIT) and endocrine system. Impaired calcium homeostasis is thought to be a consequence of iron overload seen in multi-transfused thalassemia patients. Defective synthesis of 25 OH vitamin D have been described in these patients which negatively affect their bone metabolism. Haematological disorders like thalassemia syndrome used to be a potential lethal disease previously, but advancement in therapies and optimized transfusion programs have improved quality and life expectancy of these patients.

Thalassemia is one of the most common hereditary genetic disorders in Pakistan with a very high regional and geographical prevalence. Owing to the limited sources in local set-up, thalassemia major patients undergo frequent transfusions without proper monitoring which make them prone to develop complications in the said bodily systems chiefly due to iron overload. A study depicting description of vitamin D levels in local thalassemia major population is lacking. The current study will bring forth primary details which will guide further research in this regard.

METHODOLGY

The study was commenced after approval from Advanced Studies & Research Board (ASRB) and Ethical Research Committee, KMU. It was conducted from June 2014 to December 2014. Eligible patients were identified and contacted at transfusion centers and thalassemia day care clinics of major teaching hospitals. Proper NOCs were obtained from these centers. Purpose and benefits of the study were explained to the patients and informed written consent was taken.

Patients from district Peshawar with β thalassemia syndrome, who were pre-diagnosed with β thalassemia syndrome based on electrophoresis testing, were included in the study. Patients taking vitamin D and calcium supplements were excluded from the study. Also patients with any other systemic co-morbidity and/or other chronic hemolytic anemia were not enrolled.

To measure serum vitamin D levels, Euro-Immune® 25-OH Vitamin D kit was used. The kit employs an ELISA (enzyme-linked immunosorbent assay) based technique called competitive ELISA on Rayto® microplate reader. Serum Calcium levels were measured using Calcium Ar-senazo® kit on Microlab 200®. Optimal level of vitamin D is defined as 25-OH Vit D concentration greater than 30 ng/ml, mild to moderate VDD is defined levels of 25-OH Vit D from 10-30 ng/ml, while severe deficiency is categorized as concentration of 25-OH Vit D less than 10 ng/ml.

Statistical Package for Social Sciences (SPSS) program (version 20) was used to statistically evaluate the study findings. Student t-test was posed to find similarity/difference among groups. Significance level was set at p-value of 0.05.

RESULTS

Clinical and Demographic Data

A total of 141 thalassemia syndrome patients were recruited for current study (Table 1), including 78 male and 63 female patients; 119 patients were from pediatric age group (< 18 years) and 22 were from adult group (18 years and above). The mean age of our study group patients was 12.62±5.10 years.

<table>
<thead>
<tr>
<th>Table 1 Gender-Age description of study group</th>
</tr>
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<tbody>
<tr>
<td>Age Group</td>
</tr>
<tr>
<td>----------</td>
</tr>
<tr>
<td>Males</td>
</tr>
<tr>
<td>Females</td>
</tr>
<tr>
<td>Total</td>
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ASSESSMENT OF VITAMIN D AND CALCIUM LEVELS IN MULTI TRANSFUSED B THALASSEMIA SYNDROME PATIENTS

BIOCHEMICAL STUDIES

In our study we found that the mean 25-OH Vit D levels of our study patients was 17.48±11.34 ng/dl, while mean total serum Ca concentration was 8.67±9.1 mg/ dl. Only 21.3% of our patients had optimal/normal levels of serum vitamin D concentration, while 46.1% had mild to moderate deficiency and 32.6% were absolute/severe deficient in serum 25-OH Vit D concentration. Of all, 27% of patients had low total serum calcium level while 72.3% had normal and 0.7% had high levels of their total serum calcium levels. Mean serum ferritin level

<table>
<thead>
<tr>
<th>Serum Ferritin</th>
<th>Frequency</th>
<th>Percentage (%)</th>
<th>Cumulative Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mildly Raised</td>
<td>2</td>
<td>1.4</td>
<td>1.6</td>
</tr>
<tr>
<td>Moderately Raised</td>
<td>35</td>
<td>24.8</td>
<td>28.5</td>
</tr>
<tr>
<td>Severely Raised</td>
<td>61</td>
<td>43.3</td>
<td>49.6</td>
</tr>
<tr>
<td>Very Severely Raised</td>
<td>25</td>
<td>17.7</td>
<td>20.3</td>
</tr>
<tr>
<td>Total</td>
<td>123</td>
<td>87.2</td>
<td>100.0</td>
</tr>
<tr>
<td>Missing</td>
<td>18</td>
<td>12.8</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>141</td>
<td>100.0</td>
<td></td>
</tr>
</tbody>
</table>

Table 2 Serum ferritin levels of study patients

Figure 1 Vitamin D levels in study patients

Figure 2 Serum vitamin D negatively correlates with serum ferritin levels
Figure 3 Serum total calcium levels of study patients

Figure 4 Strong positive association between serum vitamin D and serum calcium levels

was 7555±5029 ng/ml. None of the study patients had normal serum ferritin level (Table 2).

**DISCUSSION**

Our study revealed a significant prevalence (78.7%) of VDD in multi-transfused thalassemia syndrome patients of district Peshawar (Figure 1). A study conducted in North America reported VDD in 82% of study patients, with serum vitamin D levels less than 30 ng/ml. Studies from Asia revealed prevalence of VDD among thalassemia patients ranging from 37% to 100%. Prevalence of VDD in thalassemia patients from Europe has been found to vary considerably, ranging from 36% to 87%. A local cross-sectional survey in asymptomatic normal population comprised of 300 individuals, reported VDD in 84.3% of subjects with a median value of 18.8 ng/dl. This prevalence is close what we found in our study patients, however, the median vita-min D value in our study group was significantly lower (i.e. 14.5 ng/dl).

A significant negative correlation (p value 0.030) of serum vitamin D & serum ferritin concentration was found in the current study (Figure 2).
Negative correlation between ferritin and 25-OHD is found in several other ethnicities as well\(^2,25\). It is already known that high serum ferritin levels are associated with increased liver iron concentration\(^{24,32}\). Iron deposition in turn, impairs liver metabolism of 25-OHD, thus lowering vitamin D level in the body\(^{24,35}\).

Calcium levels were found to have been low in 27% of the study patients (Figure 3). A study from Turkey in 2012 reported that 27.66% thalassemia patients had low serum calcium levels\(^6\). Tantawy et al found that 75% of their study patients had low levels of serum calcium\(^{34}\). Another survey conducted at Doha, Qatar revealed that 5% of thalassemia patients had low serum calcium levels\(^{31}\). A study conducted in India in 2008 showed a mean level of 5.534±1.11 mg/dl\(^7\). Serum calcium levels were found to have been low in 27% of the study patients (Figure 3). A study from Turkey in 2013 found that mean total serum calcium level was 6.6±1.2mg/dl\(^8\). Our study findings are, thus in agreement to what has already been established earlier.

Vitamin D is primarily involved in calcium metabolism. Serum 25-OHD levels less than 30 ng/dl is associated with a significant decline in intestinal calcium absorption\(^{7,11,32}\). Without vitamin D, only 10-15% of the dietary calcium is absorbed\(^{15,16}\). A positive correlation between serum calcium and vitamin D in thalassemia patients was found in a study by Zoga et al. In our study we also found a significant positive correlation (p value < 0.001) between the two entities supporting the afore-mentioned concept (Figure 4).

Owing to lack of resources, the current study was limited to single (though largest and busiest) transfusion center from the region. High prevalence of VDD and low serum total calcium levels in our study emphasizes the importance of more detailed studies in thalassemia patients nationwide. It is recommended to monitor serum vitamin D and calcium levels routinely and commence appropriate therapy where necessary.

**CONCLUSION**

In the whole sum, our study revealed that 78.7% of local transfusion dependent B-thalassemia patients are VDD whereas hypocalcemia prevails in 27% of these patients. It was also found that high serum ferritin levels are negatively associated with serum vitamin D levels. Low calcium levels were also found to have been positively correlated to low serum vitamin D levels. It is therefore advised to monitor these vital metabolites regularly and replenish where needed.

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