Prevalence of Vitamin-D Deficiency in Patients with Acute Coronary Syndrome in Syria

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ABSTRACT

The objectives of this study were to estimate the prevalence of vitamin D deficiency in patients with acute coronary syndrome in comparison with normal individuals and study the correlation between these two conditions. We measured the plasma 25-hydroxy vitamin D (25-OH-D) levels in 60 patients with acute coronary syndromes (ACS) of both gender and in 30 age matched control individuals of both gender without any known cardiovascular or systemic diseases. The levels of 25-OH-D were measured by ELISA method and the results were statically analyzed to find out any possible correlation. We classified the cases according to their plasma 25(OH)D levels. 25(OH)D levels of ≥ 30 ng/ml were considered normal, levels < 30 and > 20 ng/ml were classified as insufficient, while levels of ≤ 20 ng/ml were classified as deficient. In the current study the prevalence of hypovitaminosis D in the patients group was much higher than it was in the control group. Vitamin D deficiency was observed in 80% and insufficiency in 13% of total patients of ACS, thereby bringing the total count to 93%. Whereas only 7% of the patients had adequate vitamin D levels. Thus, these results indicate the existence of a significant correlation between the vitamin D deficiency and ACS in comparison to healthy controls.

KEYWORDS: Vitamin D Deficiency, Cardiovascular, Acute Coronary Syndrome, Prevalence.

Introduction

Vitamin D deficiency is a worldwide health problem. A very high prevalence (96%) of vitamin D deficiency has been reported in patients with coronary artery disease (Lee et al., 2011). A growing body of evidence supports an association between vitamin D and cardiovascular disease (Welles et al., 2014). Rates of vitamin D deficiency and cardiovascular disease increase with distance from the equator, with higher rates of ischemic heart disease noted in countries with lower levels of ultraviolet B exposure (Zittermann et al., 2005). Vitamin D levels have been shown to be seasonal, with higher levels in summer (Zittermann et al., 1996), and the rate of ischemic heart disease can display similar seasonal patterns (Douglas et al., 1995). Epidemiologic studies (Grimes et al., 1996; Rostand, 1997) have reported a trend toward a higher prevalence of coronary heart disease and hypertension with increasing distance from the equator, and these higher rates are attributed to the higher rates of vitamin D deficiency in regions with less exposure to sunlight.

Vitamin D in the form of 1,25(OH)2D is a hormone, because it is produced primarily in one organ (the kidneys). Then it circulates throughout the body, where it exerts wide ranging effects. The VDR is present in most tissues, including endothelium, vascular smooth muscle, and myocardium (Zittermann, 2006). In vitro, activated 1, 25-dihydroxy vitamin D directly suppresses renin gene expression (Sigmund et al., 1990; Li et al., 2002), regulates the growth and proliferation of vascular smooth muscle cells and cardiomyocytes (O’Connell et al., 1997), and inhibits cytokine release from lymphocytes (Rigby et al., 1987). Studies in knockout mice have confirmed that the absence of vitamin D receptor activation leads to tonic upregulation of the renin-angiotensin system, along with the development of hypertension and left ventricular hypertrophy (Li et al., 2002; Wu et al., 1995; Xiang et al., 2005). Previous studies (Xiang et al., 2005; Younget al., 2011; Forman et al., 2007; Martinset al., 2007) have demonstrated associations between low vitamin D levels and increased plasma renin activity, coronary artery calcification, blood pressure, and cardiovascular diseases.

To the best of our knowledge, no study from Syria has evaluated the correlation between ACS and Vitamin D deficiency up till now. However, such data will be of immense use for the Syrian health care providers. Therefore, we designed an observational study aimed to determine the prevalence of vitamin D deficiency in patients admitted with acute coronary syndrome and to evaluate the relation between the two states.
Materials and Methods

Study Populations

We included 90 individuals in this study; 60 of them were consecutive acute coronary syndrome patients (group A) and admitted to the heart care unit at affiliated hospitals of Aleppo University in Aleppo, Syria during the period from August 2015 to December 2015. A trained data collector interviewed the participants using a structured questionnaire. Baseline clinical characteristics including socio demographic data, diabetes mellitus, hypertension, history of coronary syndrome, family history of coronary artery disease, and smoking history were obtained. The diagnosis of acute coronary syndrome was based on raised level of cardiac enzymes (CK-MB and Troponins), and electro-cardiographic (ECG) changes.

The control group (group B) consisted of 30 individuals that are age matched to the patient group. Those individuals were without any known cardiovascular diseases, hypertension, chronic diseases (such as renal or hepatic diseases), endocrine and metabolic diseases (such as diabetes mellitus (DM), hyperthyroidism or hyperparathyroidism), mal-absorption, bone disease or malignancy. Individuals who had recently received vitamin D or calcium supplements during the last three months, or received any drugs affecting vitamin D and calcium metabolism like corticosteroid, bisphosphonates and anti-epilepsy drugs were excluded from the study. All subjects were enrolled after taking a written informed/voluntary consent.

Laboratory Assays

Plasma samples were obtained immediately after admission and were frozen at −20°C until analyzed. We measured biochemical parameters including creatine kinase – MB and troponin T that were measured quantitatively by an immuno assay technology using Cobas e411 module (Roche Diagnostics, Mannheim, Germany). The 25(OH)D concentrations were measured by competitive ELISA (DiaMetra, Pozzulo, Italy). The lowest detectable concentration of 25(OH)D was 0.3 ng/ml at the 95% confidence limit. We classified the subjects according to their 25-hydroxyvitamin D levels into three groups; vitamin D-deficient, insufficient or sufficient on the basis of 25(OH)D concentrations of ≤20 ng/ml, 20-30 ng/ml or ≥30 ng/ml respectively, according to recent consensus (Dawson-Hughes et al., 2005).

Statistical Analyses

The Statistical Package for Social Sciences (SPSS version 20) was used for data analysis. The data were categorized as mean ± SD and n (%). Student’s t test for numeric variables and Pearson’s chi-square test for categorical variables were used. P value of less than 0.05 was considered to be statistically significant.

Results and Discussion

The study included 60 patients as acute coronary syndrome group (Group A) and 30 persons as control group (Group B). In the current study vitamin D deficiency was recorded in 80% and insufficiency in 13.3% of total patients of ACS taking total count to 93.3%. Whereas, only 6.7% of the patients had adequate Vitamin D levels (Figure 1).

The baseline characteristics of cases in group A and group B are presented in Table 1. The mean ages were 55.30 ± 10.40 years in group A with males’ dominance (73.3%), and 49.27 ± 9.88 years in group B with a greater proportion of women (56.7%). The mean 25(OH)D plasma concentrations were 12.34 ± 9.62 ng/mL in group A, and 21.58 ± 5.99 ng/ml in group B. Except for hypertension, diabetes mellitus and previous heart diseases, that did not exist in control group, there were significant differences in smoking, mean plasma 25-hydroxy vitamin D, Troponin T and CK-MB levels between the two groups. The prevalence of hypovitaminosis D in group A was much higher than it was in the control group and the difference was statistically significant (P<0.001) (Figure 2).

Table 1

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group A (N=60)</th>
<th>Group B (N=30)</th>
<th>P (value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>55.30 ± 10.40</td>
<td>49.27 ± 9.88</td>
<td>0.05</td>
</tr>
<tr>
<td>Male/Female</td>
<td>44 (73.3 %)/16 (26.7 %)</td>
<td>13 (43.3 %)/17 (56.7 %)</td>
<td>0.05</td>
</tr>
<tr>
<td>Hypertension</td>
<td>26 (43.3 %)</td>
<td>0</td>
<td>0.000*</td>
</tr>
<tr>
<td>Smoking</td>
<td>40 (66.7 %)</td>
<td>4 (13.3 %)</td>
<td>0.000*</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>26 (43.3 %)</td>
<td>0</td>
<td>0.000*</td>
</tr>
<tr>
<td>Previous Heart Disease</td>
<td>26 (43.3 %)</td>
<td>0</td>
<td>0.000*</td>
</tr>
<tr>
<td>Vit D (ng/ml)</td>
<td>12.34 ± 9.62</td>
<td>21.58 ± 5.99</td>
<td>0.000*</td>
</tr>
<tr>
<td>Troponin T (ng/ml)</td>
<td>1.09 ± 1.37</td>
<td>0.0036 ± 0.0010</td>
<td>0.000*</td>
</tr>
<tr>
<td>CK-MB (ng/ml)</td>
<td>12.66 ± 18.04</td>
<td>1.38 ± 1.05</td>
<td>0.001*</td>
</tr>
</tbody>
</table>

*Statistically significant difference between two groups (P<0.05).
Vitamin D is the mature hormone involved in regulation syndrome patients (group A) versus control cases (group B). Fig. 2. The mean plasma 25(OH)D concentrations in acute coronary syndrome patients (group A) versus control cases (group B).

Vitamin D is a hormone precursor as 1, 25-dihydroxy vitamin D is the mature hormone involved in regulation of mineral ion homeostasis (Bringhurst et al., 2012). The major source of vitamin D is cutaneous production. Ultraviolet radiation can change 7-dehydrocholesterol to vitamin D (Kim et al., 2008). Synthesis of vitamin D in skin depends on several factors including skin pigmentation, latitude, season, clothing, age, sunscreen use and local weather conditions (Rosen., 2011). Vitamin D can also be absorbed from both animal and plant foods in the intestine (Bringhurst et al., 2012).

Vitamin D enters the circulation and is converted to 25-hydroxy vitamin D in the liver. Measuring serum 25-hydroxy vitamin D is the most common screening test because it is the major storage form of vitamin D. Its half-life is about two to three weeks (Morazdeh et al., 2008). Currently a normal level of 25-hydroxy vitamin D is defined as a serum level of 30-76 ng/ml (75-190 nmol/l) (Rosen., 2011). 1, 25-dihydroxy vitamin D that is generated in kidneys has the greatest affinity to vitamin D receptors. Low levels of 1, 25-dihydroxy vitamin D do not mean vitamin D deficiency because it results from other causes especially renal failure (Rosen., 2011).

In the present study, we found a considerable high prevalence of vitamin D deficiency in patients with acute coronary syndrome; vitamin D deficiency was recorded in patients had adequate Vitamin D levels. This finding is in concordance to the study of (Lee et al., 2011) in Kansas, USA where in they reported a very high prevalence up to 75% as 25(OH)D deficient and 21% as insufficient, making a total of 96% of patients with abnormally low 25(OH)D levels who presented with coronary artery disease. Similarly, (Mirghani et al., 2015) in Kingdom of Saudi Arabia, reported that the majority of patients with acute coronary syndrome (87.4%) were either vitamin D deficient (62%) or insufficient (25.4%). In another study from U.K, most subjects (92%) had suboptimal levels of 25(OH) D (<75 nmol/L), with 22.2% being severely deficient (<25 nmol/L) and optimal 25(OH)D levels substantially lowered all-cause and cardiovascular diseases mortality in subjects with the metabolic syndrome (Thomas et al., 2012).

The results of the current study suggest a significant correlation (P<0.001) between the prevalence of vitamin D deficiency and ACS in comparison to healthy controls. Several mechanisms may explain the link between vitamin D deficiency and cardiovascular diseases. First, experimental studies indicate that 1,25(OH)2D participates in the regulation of renin-angiotensin axis by directly suppressing renin gene expression (Li et al., 2002; Xiang et al., 2005) Renin overexpression can be produced in wild-type mice by pharmacological inhibition of vitamin D synthesis (Li et al., 2002). Second, Putative vascular effects of vitamin D are wide ranging and include modulation of smooth muscle cell proliferation (Mitsuhashi et al., 1991), inflammation (Rigby et al., 1987), and thrombosis (Aihara et al., 2004). Vascular smooth muscle cells and endothelial cells express receptors for vitamin D and have the ability to convert circulating 25(OH)D to 1,25(OH)2D. (Somjen et al., 2005; Zehnder et al., 2002). Third, vitamin D deficiency causes secondary hyperparathyroidism (Wallis et al., 2008; Lee et al., 2008) acting through pathogenic pathways associated with parathyroid hormone (PTH) excess (Lee et al., 2008): (1) increased insulin resistance and pancreatic β-cell dysfunction, predisposing to the metabolic syndrome and diabetes; (2) activation of the renin-angiotensin system, increasing blood pressure and leading to left ventricular hypertrophy (with subsequent apoptosis and fibrosis); and (3) stimulation of systemic and vascular inflammation, augmenting atherogenesis.

The results of the current study are similar to previous studies in other countries. According to NHANES 2001–2004, vitamin D deficiency was more prevalent in persons with cardiovascular diseases and cardiovascular diseases were more common in adults with lower 25-hydroxy vitamin D (Kim et al., 2008). Multiple studies have evaluated the relation of vitamin D prospectively with long-term cardiovascular outcomes in subjects with no histories of cardiovascular disease. In dialysis patients, those who were vitamin D deficient were at significantly increased risk for early mortality (Wolf et al., 2007). Supplementation has been reported to reduce this risk (Wolf et al., 2007; Teng et al., 2005). Similarly, in healthy male health professionals aged 40 to 75 years with no histories of coronary artery disease, vitamin D deficiency (25(OH)D <15 ng/ml) was associated with a two fold increased rate of myocardial infarction over a 10-year period (Giovannucci et al., 2008). In the Framingham Offspring Study (Wang et al., 2008), subjects with no histories of cardiovascular disease and severe vitamin D deficiency (25(OH) D<10 ng/ml) had an increased risk for developing the first cardiovascular event after 5 years of follow-up compared with subjects with of 25(OH)D levels of >15 ng/ml (hazard ratio 1.80, 95% confidence interval 1.05 to 3.08). In more than 3,000 subjects who had undergone coronary angiography, those with severe vitamin D
deficiency (<10 ng/ml) had 3 to 5 times the risk for death from sudden cardiac death, heart failure, or fatal stroke during a 7-year follow-up period compared to those who had optimal levels (>30 ng/ml) (Pilz et al., 2008(b); Pilz et al., 2008(a)). Finally, the potential to reduce mortality with vitamin D supplementation in diverse populations was supported by a meta-analysis of 9 studies of varying sizes and designs (Autier and Gandini., 2007).

Conclusions

In conclusion, our data indicate a very high prevalence of vitamin D deficiency in patients admitted with acute coronary syndrome, and significant correlation between the prevalence of vitamin D deficiency and occurrence of acute coronary syndrome in comparison to healthy controls in the Syrian population.

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References


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