Correlation of serum vitamin D levels with disease activity in ankylosing spondylitis

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Abstract

Purpose: The purpose of this study was to assess the correlation of serum vitamin D levels with disease activity in Ankylosing spondylitis patients.

Type of Study: Hospital Based Cross Sectional study.

Methods: Fifty patients of ankylosing spondylitis and fifty apparently healthy controls were enrolled in study from October 2015 to May 2017. Bath AS Disease Activity Index (BASDAI), erythrocyte sedimentation rate (ESR), C reactive protein, Ankylosing spondylitis disease activity score (ASDAS), Serum 25hydroxyvitamin D (25OHvitD) were assessed in Ankylosing spondylitis patients. Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean ± SD. Pearson`s and spearman`s correlation coefficient were used to analyse relationship between Vitamin D and Disease activity.

Results: The patient population studied, had an average age of 31 .23 ± 6.34 (mean ± SD) years (range 18-45 years). In our study in group 1(cases)**:** 37 (74 %) cases had Serum 25-OH Vit D levels < 30 nmol/L i.e. Vitamin D deficiency. Mean serum levels were 23.04 nmol/L ± 14.9. In group 2(controls)**:** 11(22%) controls had Vitamin D deficiency. Mean serum levels were 48.6 nmol/L ± 24.69. Within group 1, patients with inactive disease (ASDAS <1.3) had vitamin D level 46.8 nmol/L and moderately active disease (ASDAS 1.3-2.0) had vitamin D level of 25.98 ±8.86 nmol/L, high activity group (ASDAS 2.1-3.5) had 18.21±12.03 and very high activity group (ASDAS > 3.5) had 11.18±4.3 nmol/L. Serum 25 OH Vitamin D levels showed moderate inverse linear relationship with ASDAS (coefficient of correlation = -0.642) in our study.

Conclusion: Serum Vitamin D levels were low in patients of AS compared to normal healthy controls and disease activity of AS inversely correlates with level of serum vitamin D levels.

Keywords: Ankylosing Spondylitis, Disease activity, Serum Vitamin D, Autoimmune, Correlation.

Introduction

Ankylosing Spondylitis is the prototype of the spondyloarthropathies, a family of related disorders that are linked by common genetics (the human leukocyte antigen class-I gene HLA-B27) and a common pathology (enthesitis).[1] AS is a chronic, multisystem inflammatory disorder primarily involving the sacroiliac (SI) joints and the axial skeleton. AS usually begins in the second or third decade and rarely after age of 45 years.[2,3] The primary pathology of the spondyloarthropathies is enthesitis with chronic inflammation, including $CD4^+$ and $CD8^+$ T lymphocytes and macrophages, leading to fibrosis and ossification at sites of enthesitis[2].Diagnosis of Ankylosing Spondylitis is made using new criteria proposed by the Assessment of Spondyloarthritis International Society (ASAS).[2] Measurement of disease activity of AS can be measured with nonspecific inflammatory serum markers, such as C-reactive protein(CRP) an erythrocyte sedimentation rate(ESR) and the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)[4,5] and Scoring of Disease Activity is done using Ankylosing Spondylitis Disease Activity Score.[6,7,8]

VITAMIN D (1,25-dihydroxyVitamin D) is the major steroid hormone involved in mineral ion homeostasis regulation. Studies have shown that vitamin D influences both the innate and adaptive immune systems.[9] Thus it stands to be a reason that Vitamin D may play a role in the development and progression of AS. Treatment in AS is mainly symptomatic and only few drugs actually slow the disease process. Therefore, exploring whether Vitamin D influences the disease process is important, as this could highlight new or adjunct treatment options.[11]

Materials and Methods

Patients: The study was conducted at Central Institute of Orthopaedics, Vardhman Mahavir Medical College and Safdarjung hospital, New Delhi. Between October 2015 to May 2017, 50 patients who visited OPD central institute of orthopaedics, VMMC and Safdarjung hospital with complaints of lower back pain for more than three months, were evaluated clinically and radiologically and those patients fulfilling the ASAS criteria were diagnosed with Ankylosing Spondylitis (Cases) were grouped together in group 1 (cases). Excluded were patients with concomitant presence of inflammatory bowel disease, chronic renal or hepatic disease, diabetes mellitus, thyroid or parathyroid disease or drug intake affecting bone metabolism (bisphosphonates, glucocorticoids, anticonvulsants, diuretics or coumarin derivatives). Apparently healthy age, sex and ethnicity matched people visiting OPD

during the same period were recruited as controls in group 2. The study was approved by the local ethical committee and all patients provided written consent to participate in study.

Clinical and Laboratory assessments: In Both the groups Serum levels of 25hydroxy vitamin D were measured using RIA (radioimmuno assay). Disease activity of AS was evaluated using Bath Ankylosing Spondylitis Disease activity index (BASDAI; on a scale of 0-10), ESR, CRP and ASAS endorsed disease activity score (ASDAS) calculated from BASDAI questions 2,3,6 and CRP. Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean ± SD and to study relationship between variables Spearman correlation coefficient was measured.

Results

Mean Age of 50 AS patients was 31.23 ± 6.34 years and median duration of disease was 2.3 years (range 9 months to 6 years) and 76% were males.90% patients were positive for HLAB27.

Out of AS patients 98 % had BASDAI ≥ 4 and 86 % had elevated ESR and 90 % had elevated CRP.

Prevalance of Vitamin D Deficiency: In our study in group 1(cases)**:** 37 (74 %) cases had Serum 25-OH Vit D levels < 30 nmol/L i.e. Vitamin D deficiency. Mean serum levels were 23.04 nmol/L ± 14.9. In group 2(controls)**:** 11(22%) controls had Vitamin D deficiency and mean serum levels were 48.6 nmol/L ± 24.69.

Vitamin D and Disease Activity of AS: AS patients with inactive disease (ASDAS <1.3) had vitamin D level 46.8 nmol/L and moderately active disease (ASDAS 1.3-2.0) had vitamin D level of 25.98 ±8.86 nmol/L, high activity group (ASDAS 2.1-3.5) had 18.21±12.03 and very high activity group (ASDAS > 3.5) had 11.18±4.3 nmol/L. Serum 25 OH Vitamin D levels showed moderate inverse linear relationship with ASDAS (coefficient of correlation = -0.642) in our study.

Discussion

AS is most common among all spondyloarthropathies and is a chronic, multisystem inflammatory disorder primarily involving the SI joints and the axial skeleton with frequent extraosseous involvement.[2,3] The pathogenesis of AS is poorly understood. However recent studies have shown immune mediated mechanisms involving human leucocyte antigen HLA-B27, inflammatory cellular infiltrates, cytokines, and genetic and environmental factors are thought to have key roles.

Vitamin D is a steroidal hormone that has many diverse biological actions in number of target tissues. The primary function of Vitamin D are Calcium metabolism and regulation of bone metabolism.

Recent studies have shown that Vitamin D influences both the innate and adaptive immune systems. Cells of the innate immune system (monocytes/macrophages and dendritic cells) express 1-alpha-hydroxylase (CP27B) and Vitamin D receptor (VDR) and utilize Vitamin D for autocrine responses. In the adaptive immune system, 1,25-dihydroxy Vitamin D reduces Th1 and Th17 cell activity and supports Th2 and regulatory T cells that increase immune tolerance.1,25-dihydroxy Vitamin D also reduces B cell proliferation and differentiation. These actions of Vitamin D make it a potentially important modulator of autoimmunity.[17,18]

In Our Cross Sectional Study 37 (74 %) AS patients had Serum 25-OH Vit D levels < 30 nmol/L i.e. Vitamin D deficiency. Mean serum levels were 23.04 nmol/L ± 14.9. AS patients with inactive disease (ASDAS <1.3) had vitamin D level 46.8 nmol/L and moderately active disease (ASDAS 1.3-2.0) had vitamin D level of 25.98 ±8.86 nmol/L, high activity group (ASDAS 2.1-3.5) had 18.21±12.03 and very high activity group (ASDAS > 3.5) had 11.18±4.3 nmol/L. Serum 25 OH Vitamin D levels showed moderate inverse linear relationship with ASDAS (coefficient of correlation = -0.642) in our study.

In a study by Lange et al. in 2001 while investigating relation between disease activity in AS and vitamin D found that high disease activity and decreased vitamin D levels were associated with increased bone resorption[12].

In a study by Baskan et al. in 2009 while studying relation between osteoporosis and vitamin D and disease activity in AS with 100 AS patients found that vitamin D levels were lower in AS patients and suggested that monitoring vitamin D levels would be useful in determining osteoporosis risk in AS patients.[13]

In a study by Zhang et al. in 2014 while assessing serum vitamin D and ICTP levels in 150 AS patients found that high incidence of vitamin D inadequacy in AS patients and suggested that serum vitamin levels may play important role in pathophysiology of AS.[14]

In a meta-analysis by Pokhai et al in 2014 while reviewing 8 studies, found that 5 of 8 studies had shown that AS patients had significantly lower Vitamin D levels than controls, while 3 studies found no significant difference and reported that these findings correspond with other cross sectional studies which showed that deficient serum levels of vitamin D are present in significant percentage of patients with autoimmune diseases.[15]

Recently in a meta-analysis by Cai et al in 2015 involving all studies on AS patients published before june 2014 in pubmed reviewed Vitamin D in AS patients and revealed that there is a consistent and inverse relationship between serum vitamin D levels and AS disease activity and suggested that further well

designed large studies are required to confirm these findings.[16]

Our study like previous studies had reported that Serum Vitamin D levels were low in patients of AS compared to normal healthy controls and disease activity of AS inversely correlates with level of serum vitamin D levels. However longitudinal study with large sample size is needed to confirm this correlation.

Conclusion

1. Vitamin D levels are lower in AS patients than in healthy controls.
2. Vitamin D level is inversely correlated with several markers of AS disease activity.
3. Monitoring of Vitamin D level should be done in AS patients with higher disease activity.
4. Further large well designed longitudinal study to determine susceptibility of AS in vitamin D deficient patients.
5. Further large well designed longitudinal study to determine association of vitamin D levels and disease activity in AS patients.

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