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To Study The Serum Vitamin –D And Oxidative Stress Status In **Rheumatoid Arthritis**

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ARTICLE INFO

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Keywords:Rheumatoid arthritis,oxidativestress,vitamin -D

ABSTRACT

Aim and objectives: Rheumatoid arthritis (RA) is a chronic autoimmune systemic disease characterized predominantly by synovial inflammation, leading to joint destruction. The study was undertaken to analyze the vitamin -D and oxidative stress status in Rheumatoid arthritis

Materials and methods: The Study includes Patients diagnosed as RA by using RA factor within the age group of 30 to 60 years and comprised of 20 age matched control group. To assess oxidative stress, serum Malonyldialdehyde (MDA) was by thiobarbituric acid method and antioxidant level was assessed by estimation of serum vitamin C by dinitrophenyl hydrazine method. And vitamin D total is estimated by chemiluminescent immunoassay.

Results: There is a significant decreased level of vitamin -D in the RA patients (37.58±5.7ng/ml) as compared to healthy controls (58.5±5.6ngl/ml). There is a a significant increased levels of MDA in the RA patients (7.6±1.09) as compared to healthy controls (8.4±2.8). There is a significant decreased level of vitamin -c in the RA patients (0.6±0.3mg/dl) as compared to healthy controls (1.0±0.31mg/dl).

Conclusion: Low levels of Vitamin D deficiency in RA patients is associated with inflammation which leads to Increased oxidative stress status , which may lead to connective tissue degradation leading to joint and periarticular deformities in rheumatoid arthritis.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic autoimmune systemic disease characterized predominantly by synovial inflammation, leading to joint destruction. RA affects up to 1% of the population in the world and is associated with reduced life expectancy (1). Rheumatoid arthritis (RA) is an autoimmune disease of unknown aetiology [2]. Both T and B lymphocytes are involved in the pathogenesis of the disease [3]. The role of T lymphocytes as well as that of B lymphocytes in the pathogenesis of RA has been further proved by the therapeutic efficacy of methods affecting both T and B lymphocytes, namely the biological agents [4]. Rheumatoid arthritis is a whole body disorder, primarily affecting the synovial joints. Early changes include inflammation and thickening of the synovial membrane. Late changes include destruction of the cartilage along with formation and deposition of pannus in the joint spaces. The

inflammation and various symptoms such as fever, loss of weight and weakness is due to the release of a chemical mediator called cytokines. The etiology of the disease could be attributed to genetic and environmental factors; the exact cause is still unknown. Vitamin D could be one of the environmental factors linked to rheumatoid arthritis. (5) Vitamin D is a steroid hormone involved in bone and calcium metabolism. It is involved in the regulation of calcium homeostasis, as it regulates calcium absorption from the gastrointestinal system [6]. The hormone is synthesized in the skin by the action of ultraviolet irradiation [7]. Vitamin D, as a prohormone, is considered to be able to play potential immune-suppressive roles and to

exert an endocrine action on the immune system cells, generating anti-inflammatory and immunoregulatory

effects [8]. Vitamin D deficiency may increase the risk for

the development of RA [5]. The role of vitamin D deficiency Author(s) agree that this article remain permanently open access under the terms of the **Creative Commons Attribution License 4.0 International License**

in the pathogenesis of RA, as well as the relationship between vitamin D deficiency and the activity of RA is discussed [9]. Epidemiological data also imply that vitamin D deficiency may be a risk for development of autoimmune and other chronic diseases [10,11]. Preliminary studies suggest that low levels of vitamin D may be common in rheumatoid arthritis (RA) [12-15]. More recently, vitamin D deficiency was found in 42 out of 145 postmenopausal women with RA in the USA, with the highest prevalence among African Americans [16,17]. Moreover, some authors reported an inverse relationship between serum levels of vitamin D metabolites and disease activity or disability in patients with RA or early inflammatory polyarthritis, although conflicting results have been found [18]The relationship between RA and vitamin D has been extensively studied, and the results remain controversial. Several studies show that RA patients have lower levels of vitamin D [19,20]. T-cells and cytokines play an important role along with oxygen radicals as superoxide and hydrogen peroxide released by activated macrophages in the progression of rheumatoid arthritis .These reactive oxygen species (ROS) and reactive nitrogen species (RNS) which are thus produced have both beneficial and toxic effects Oxidative stress is the condition when concentration of ROS and RNS becomes deleterious and damage the cells and biological macromolecules and thus the body. Oxidative stress occurs due to disturbed balance between body's antioxidant mechanisms and oxidative stress production and has important role in the development of chronic disease as autoimmunity like RA, cancer etc. [21]. The objective of the study was to evaluate the relationship between vitamin D and RA, as well as the relationship between cxidativestress in RA

Materials and Method:

The study was carried out at Rajiv Gandhi Institute Of Medical Sciences & general hospital, Srikakulam, Andhra Pradesh in collaboration with Department of Orthopaedics. The Institutional Ethics Committee approved the study protocol. . The Study includes Patients diagnosed as RA by using RA factor within the age group of 30 to 60 years and comprised of 20 age matched control group. Exclusion criteria were smoking, alcohol intake, narcotic drugs, hypothyroidism, hypertension, diabetes mellitus, hyperthyroidism and any other form of arthritis except RA The study protocol was explained in detail to all the subjects and informed written consent regarding participation in the study was obtained from them. Then 5 ml of blood sample was obtained from the participant under all aseptic precautions. oxidative То assess stress. serum Malonyldialdehyde (MDA) was by thiobarbituric acid method and antioxidant level was assessed by estimation of serum vitamin C by dinitrophenyl hydrazine method. And vitamin D total is estimated by chemiluminescent immunoassay .Serum MDA level , serum vitamin C and vitamin -d levels were compared by applying unpaired t test.

Results

Table 1 shows a significant (p=0.001) decreased levels of vitamin -D in the RA patients (37.58±5.7ng/ml) as compared to healthy controls (58.5±5.6ngl/ml). vitamin -D

	parameter	Controls	Cases	p value
	Vitamin –D	58.5 ±5.6	37.58±5.7	0.001*
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levels show statistically significant decreased in cases compared to controls (p=0.0001).

Table 1: SHOWING THE MEAN VALUES OF VITAMIN -D INCONTROLS AND RA

Table 2 shows a significant (p=0.001) increased levels of MDA in the RA patients (8.4±2.8) as compared to healthy controls (3.7 ±2.8). MDA levels show statistically significant increased in cases compared to controls (p=0.0001).



Table 2: SHOWING THE MEAN VALUES OF MDA INCONTROLSAND RA

Parameter	Controls	Cases	p value
MDA	3.7 ±2.8	8.4±2.8	0.001*

Table 3 shows a significant (p=0.001) decreased levels of vitamin -c in the RA patients (0.6±0.3mg/dl) as compared to healthy controls (1.0±0.31mg/dl). vitamin -c levels show statistically significant decreased in cases compared to controls (p=0.0001).

Table 3: SHOWING THE MEAN VALUES OF MDA INCONTROLS AND RA

Parameter	Controls	Cases	p value
VITAMIN –C	1.0±0.31	0.6±0.3	0.001*



Discussion

In the present study vitamin D levels were found to be low in a group of patients with RA. Vitamin D levels have been studied in RA were found to be negatively correlated with disease activity in RA., Vitamin D deficiency may be associated with an increased risk for the development of RA. Rossini and colleagues found an inverse association between vitamin D levels and disease activity in RA [Rossini et al. 2010]. Welsh and colleagues and Kerr and colleagues found that vitamin D deficiency is linked with disease activity in. Vitamin D is known to induce immunologic tolerance [22]. Cutolo et al. reported a significant inverse association between 25(OH)D and DAS28 in patients with active RA and Patel et al. found an inverse relationship between 25(OH)D levels and tender joint count, DAS28, and HAO score only at disease onset, but not in patients with a disease duration longer than one to two year Thus, vitamin D deficiency may perturb immune tolerance and induce the development of autoimmune diseases, such as RA.[23,24] Vitamin D has immunomodulatory properties, acting on the immune system both in an endocrine and in a paracrine manner [25]. There was a negative relationship between vitamin D levels and RA disease activity in our study. It appears to regulate the immune response by a variety of mechanisms, such as decreasing antigen presentation [Bartels et al. 2010], inhibiting the proinflammatory T helper type 1 profile [Jirapongsananuruk et al. 2000] and inducing regulatory T cells [Correale et al. 2009]. 1,25(OH)2D3 suppresses proliferation and immunoglobulin production and retards differentiation of B-cell precursors into plasma cells [Chen et al. 2007]. These data support a role for vitamin D deficiency in the development and progression of autoimmune inflammatory conditions in general, and in particular RA

Oxidative stress being one of the important cause of various rampant diseases of modern age such as RA, cancer, osteoarthritis, osteoporosis and atherosclerosis, occurs due to the disruption of balance between body's oxidants load and antioxidants reservoir [26, 27]. RA is a inflammatory autoimmune disorder .with synovial proliferation, destruction of bone and cartilage degradation. Although the etiology of RA is still not very much clear but one recent study clearly demonstrates the involvement of reactive oxygen species in the pathogenesis of the disease. Macrophages and polymorphonuclear cells present at the site of synovitis promotes the formation of reactive oxygen species and subsequent activation of inflammatory molecules which are involved in the progression of RA[28]

In our study MDA levels were found to be significantly (P P<0.001)elevated in the patients with RA compared to the controls. Our study supports to other studies where higher MDA levels have been reported in patients with RA[29,30,31] .In other studies Kamanli A et.al there is an elevated levels of MDA has been found in the serum, plasma and erythrocytes of RA patients [32]. Sarban S et.al there is an elevated levels of MDA has been found in the serum, plasma and erythrocytes of RA patients.[33] Hassan MQ, there is an elevated levels of MDA has been found in the serum, plasma and erythrocytes of RA patients.[34] We observed significantly low levels of antioxidants vitamin C[P<0.001]in RA patients as compared to healthy individuals. In the inflamed joint, hypoxia-reperfusion occurs which may result in increased lipolysis. During this process, some lipids may get oxidatively modified by free radicals and removed by macrophages.[35] Patients with inflammation of the synovial membrane respond relatively frequently by a reduction of indicators of antioxidants and antioxidant enzymes.[36] Our results are in agreement with other recent studies that indicate that oxidative stress generated within an inflamed joint can produce connective tissue destruction leading to joint and periarticular deformities in RA.[37–39] The level of oxidative stress is found to be much higher in patients with active disease. Further indepth knowledge about this aspect of RA.

Conclusion: our findings confirm Vitamin D deficiency in RA patients, and its association with inflammation which leads to Increased oxidative stress status , which may lead to connective tissue degradation leading to joint and periarticular deformities in rheumatoid arthritis.

Funding : This research did not receive any specific grant from any funding agency in the public, commercial or not-for-profit sector.

Declaration of interest: The authors declare there exist no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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