

## Serum Vitamin D Level and it's Clinical Correlation with Rheumatological Diseases

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### Abstract

**Introduction:** Vitamin D deficiency or insufficiency is a worldwide problem including Bangladesh. It is common in Rheumatological diseases.

**Objectives:** To find out the clinical correlation of serum Vitamin D level with Rheumatological diseases.

**Materials and Methods:** This was a hospital based case control study. It was conducted in Rheumatology department of Combined Military Hospital Dhaka. Total 100 patients having Rheumatological diseases and 100 age and sex matched healthy control were included in the study. Data were collected from face to face interview, clinical examination and relevant investigation reports and processed with SPSS version 20 and obtained in tables and charts.

**Results:** Among 100 study patients' Osteoarthritis (OA) were 24(24.0%), Rheumatoid arthritis (RA) 20(20.0%), SLE 16(16.0%), Osteoporosis 16(16.0%), Ankylosing spondylitis (AS) 10(10.0%), Chikungunya arthritis (CS) 4(4.0%) and other arthritis 10(10.0%). Among patients group 84(84.0%) had vitamin D deficiency/insufficiency, of whom OA were 20(23.80%), RA 16(19.04%), SLE 16(19.04%), osteoporosis 14 (16.66%), AS 8(9.52%), CS 2(2.38%) and other arthritis 8(9.52%). Abnormal vitamin D level were in SLE 16(100.0%), osteoporosis 14(87.50%), OA 20(83.33%), RA(80.0%), AS 8(80.0%), CS 2(50.0%), and other arthritis 8(80.0%). In study patients, 60 had adequate sun exposure of whom 48(72.07%) had low serum vitamin D level and 40 had inadequate sun exposure of whom 36 (90.0%) had low vitamin D level that reflects sunlight exposure affects vitamin D status. Abnormal serum vitamin D level was more common in Rheumatological diseased patients than healthy group ( $p < 0.01$ ).

**Conclusion:** Abnormal vitamin D level were more in Rheumatological diseases than healthy control group that was statistically significant; it was also affected by lifestyle of patients.

**Key-words:** Vitamin D, Rheumatological disease. Systemic Lupus Erythematosus.

### Introduction

Vitamin D is a steroid hormone that plays essential roles in calcium and phosphate metabolism, bone formation and mineralization. It has been appreciated for its role in calcium homeostasis and bone<sup>1</sup> health since its identification in 1921. Vitamin D also has immune-regulatory role and affects both the innate and adaptive immune system cells contributing to the immune-tolerance of self-structures<sup>2</sup>. Vitamin D is synthesized in vivo when solar ultraviolet B (UVB) radiation interacts with the precursor molecule, 7-dehydrocholesterol in the skin<sup>1</sup>. The other important source of vitamin D is dietary intake and supplementation. After synthesis of vitamin D in the skin in response to ultraviolet radiation or absorption from diet, it is transported to the liver, where it undergoes 25-hydroxylation and forms 25-hydroxyvitamin D. This metabolite is the major circulating form of vitamin D. The final step in hormone activation, 1 $\alpha$ -hydroxylation, occurs in the kidney and forms<sup>1</sup>, 25-dihydroxyvitamin D, active form of vitamin D<sup>3</sup>. A 25(OH)D concentration <50 nmol/L is considered vitamin D deficiency, whereas concentration 51–74 nmol/L is considered insufficiency of vitamin D and concentrations  $\geq 75$  nmol/L are considered to be sufficient<sup>4</sup>.

Endogenous production of Vitamin D is estimated to account for 90% of total vitamin D in healthy individual, and any activity that reduces sunlight exposure will tend to reduce vitamin D level<sup>5</sup>. Aging is also associated with decreased concentrations of 7-dehydrocholesterol, the precursor of Vitamin D<sub>3</sub> in the skin and they have a 75% reduced capacity to make vitamin D<sub>3</sub> in the skin<sup>3</sup>. Other causes of vitamin D deficiency are associated with nutritional deficiency, obesity, lipid disorders and medications including antiepileptic drugs, glucocorticoids and fat malabsorption<sup>6</sup>.

Low vitamin D status is reported in many inflammatory rheumatic conditions. Vitamin D acts on a number of cells involved in both innate and acquired immunity biasing the adaptive immune system away from the Th17 and Th1, towards

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Th<sup>2</sup> and Tregs (Regulatory T cells). Deficiency accordingly could encourage autoimmunity. Vitamin D deficiency may be an important factor in autoimmune rheumatic disease such as Rheumatoid arthritis (RA), Systemic lupus erythematosus (SLE), systemic sclerosis etc. It has also possible role in initial disease development and worsening the diseases once present<sup>7</sup>. An inadequate level of vitamin D has been linked to a number of other diseases including metabolic disorders, other autoimmune conditions, as well as osteoporosis and osteomalacia<sup>8</sup>. Vitamin D has immunoregulatory activity which is mediated through VDRs present on antigen presenting cells, activated-T lymphocytes and activated-B lymphocytes. Various studies done so far suggest that vitamin D deficiency increases the risk of developing autoimmune diseases including RA and SLE. In Bangladesh, well documented data regarding correlation of vitamin D status in relation to Rheumatological diseases is presently scarce. In current study we have tried to correlate vitamin D level in patients of common Rheumatological diseases as well as in healthy control group.

## Materials and Methods

The aim of this study was to correlate vitamin D status in patients with musculoskeletal diseases like osteoarthritis (OA), SLE, ankylosing spondylitis (AS), RA, osteoporosis and other Rheumatological diseases and comparing vitamin D status with healthy individuals. This study was a hospital based case control study, carried out in Rheumatology department of Combined Military Hospital (CMH) Dhaka cantonment from July 2017 to June 2019. Total 100 patients having any Rheumatological disease or patients presented with clinical, laboratory and imaging evidences suggesting Rheumatological disease were included in the study group. Hundred age and sex matched healthy individuals were also investigated for vitamin D level as control group. Critically ill patients, extremes of age (<16 and >80 years), pregnancy, currently vitamin D supplementation and know chronic liver disease and chronic kidney disease patients were excluded from the study. Verbal consents were taken and all patients were interviewed face to face as per questionnaire and clinical examination and investigations were done. Data was collected and analyzed by using SPSS 20 and formulated in tables and charts.

## Results

Patients demographic profile of study group shown in Table-I. Among 100 patients, 60(60.0%) used to expose under sun regularly and 40 (40.0%) irregularly/ inadequately; 48(48.0%) used Bhurkha/veil, 34(34.0%) smoker, 7(7.0%) took tobacco in other forms and 3(3.0%) used to take alcohol. Presenting complains of study patients; arthralgia 96(96%),

backache 74(74%), joint swelling 66(66%), morning stiffness 64(64%), myalgia 56(56%), bone pain 54(54%), skin rash/lesion 30 (30%), restricted joint movement 24(24%), weight loss 16(16%), joint deformity 12(12%), extra-articular features 10(10%). Among 100 patients, Osteoarthritis were 24(24.0%), Rheumatoid arthritis 20(20.0%), SLE 16(16.0%), Osteoporosis 16(16.0%), Ankylosing spondylitis 10(10.0%), Chikungunya arthritis 04(4.0%) and 10(10.0%) other arthritis (Table-II). Figure-1 shows comparison of vitamin D status in between study group and healthy group; in study group deficient were in 12(12.0%), insufficient 72(72.0%) and sufficient 16(16.0%), whereas in healthy control group deficient were in 4(4.0%), insufficient 46(46.0%), sufficient 50(50.0%). Total abnormal values were found in 84(84%) in study group and 50(50%) in control group. Among 100 patients having Rheumatological diseases 84(84%) had vitamin D deficiency/insufficiency. Hundred percent of SLE patients, 87.50% of osteoporosis, 83.33% of osteoarthritis, 80% of RA, AS and other arthritis, 50% of Chikungunya had low levels of vitamin D (Table-III). Among 84 patients who had abnormal vitamin D level (deficient and insufficient) female were 60(71.43%) and 24(28.57%) male (Figure-2). Among 100 study patients, 60 had adequate sun exposure of whom 48(80.0%) had low serum vitamin D level and 40 had infrequent/ inadequate sun exposure of whom 36 (90.0%) had low vitamin D level that reflected sunlight exposure affects vitamin D status (Table-IV). Rheumatological diseases patients had abnormal serum vitamin D level in comparison to healthy control group and it was statistically significant ( $p < 0.01$ ).

**Table-I:** Demographic profile of study population (n=100)

	Variables	Frequency	Percentage
Age in years	<20	05	05
	20-30	15	15
	31-40	18	18
	41-50	16	16
	51-60	20	20
	>60	26	26
Gender	Female	72	72
	Male	28	28
Religion	Muslim	92	92
	Hindu	8	8
Residence	Urban	56	56
	Rural	44	44
Occupation	Housewife	32	32
	Retired	28	28
	Service	22	22
	Others	12	12
Sun exposure	Adequate	60	60
	Inadequate	40	40
Using Bhurkha/veil		48	48
Using tobacco	Smoking	34	34
	Smokeless tobacco	07	07
Alcoholism		03	03
Total		100	100

**Table-II:** Distribution of Cases by presenting complaints and type of diseases (n=100)

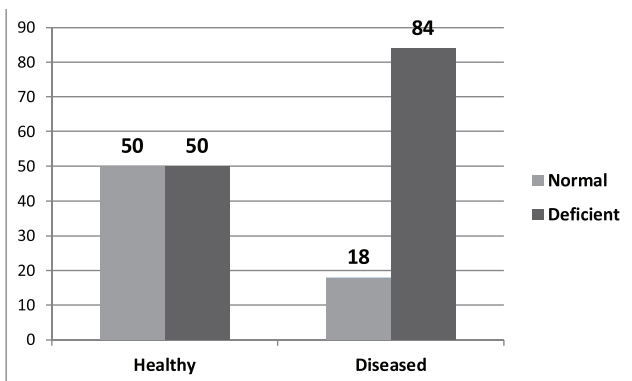
Characteristics		Frequency	Percentage	
Presenting complaints	Arthralgia	96	96	
	Backache	74	74	
	Joint swelling	66	66	
	Morning stiffness	64	64	
	Myalgia	56	56	
	Bone Pain	54	54	
	Skin Rash/lesion	30	30	
	Restricted joint movement	24	24	
	Weight loss	16	16	
	Joint deformity	12	12	
	Other Extra-articular feature	10	10	
	Total	100	100	
	Type of Diseases	Osteoarthritis	24	24.0
		Rheumatoid arthritis	20	20.0
SLE		16	16.0	
Osteoporosis		16	16.0	
Ankylosing arthritis		10	10.0	
Chikungunya arthritis		04	4.0	
Other arthritis		10	10.0	
Total		100	100	

**Table-IV:** Correlation of sun exposure to low vitamin D in study patients(n=100)

Sun exposure	Total subject	Low vitamin D level	
		Frequency	Percentage
Adequate	60	48	80
Inadequate	40	36	90

**Table-V:** Summary of vitamin D status in study group and control group

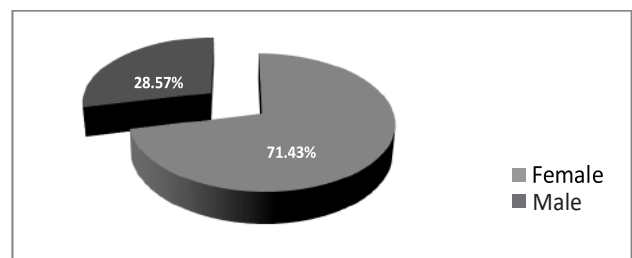
Group of Patient	Abnormal Value n (%)	Normal Value n (%)	Statistics
Study Group	84 (84)	16 (16)	$\chi^2=8.283$ $df = 1$ $p < 0.01$
Control Group	50 (50)	50 (50)	
Total	134 (67)	66 (33)	



**Figure-1:** Comparison of vitamin D status in patients of study group and healthy control group (n=100 each)

**Table-III:** Disease wise vitamin D deficiency and insufficiency in study patients (n=84)

Diseases	No of cases	Vitamin D deficiency/ insufficiency	Percentage (%)
SLE	16	16	100
Osteoporosis	16	14	87.50
OA	24	20	83.33
RA	20	16	80.0
AS	10	8	80.0
Chikungunya arthritis	4	2	50.0
Other arthritis	10	8	80.0
Total	100	84	84.0



**Figure-2:** Sex distribution of abnormal serum Vitamin D in study group (n=84)

### Discussion

Vitamin D deficiency is a global health problem caused mainly by insufficient exposure to sunlight. It is now recognized as a pandemic. No one is immune from vitamin D deficiency, both children and adults living in the United States, Europe, Middle East, India, Australia, and Asia including Bangladesh. Studies suggest that upwards of 30–50% of children and adults are at risk of vitamin D deficiency<sup>9</sup>. In other study<sup>10</sup> from Dhaka, it was found that, in Bangladesh vitamin D insufficiency (<40nmol/l) was common (80%) regardless of age, lifestyle and clothing. In another study<sup>11</sup> from Bangladesh, it was observed that women of Bangladesh were at risk of hypovitaminosis D. Seventy percent of women from low economic group and 12 percent of high economic group had serum vitamin D concentration <25 nmol/L and hypovitaminosis D ( $\leq 37.5$ nmol/L) was observed in 50% and 38% subjects in low and high economic group respectively. Rheumatological disorders are very common disorder worldwide. Some of the Rheumatological disorders such as SLE, RA and other autoimmune disorders have causal relation with low Vitamin D level and also might have role on disease activity. Vitamin D level is particularly important as its deficiency is highly prevalent in this group<sup>12</sup>. Vitamin D seems to interact with the immune system through its action on the regulation and differentiation of cells such as lymphocytes, macrophages, natural killer cells, besides interacting in the production of cytokines<sup>13</sup>. Systemic lupus erythematosus, a systemic autoimmune disorder, can cause chronic inflammation and damage in several tissues and organs<sup>14</sup>. Evidences suggest that vitamin D plays an important relationship in the pathogenesis and progression of SLE<sup>15</sup>. Vitamin D inadequacy is highly prevalent in SLE patients due to the avoidance of sunshine, photo protection, renal insufficiency and the use of medications such as glucocorticoids, anticonvulsants, antimalarials and the calcineurin inhibitors which alter the

metabolism of vitamin D or down regulate the functions of the vitamin D receptor<sup>16</sup>. Continuance insufficiency of vitamin D results in rickets and osteomalacia with skeletal deformities in children and bone pain and increased risk of fractures in adults<sup>17</sup>. The risk of osteoporosis and bone fracture is also higher in patients with SLE<sup>18</sup>.

In current study, we found that vitamin D deficiency/insufficient were more common in study patients than healthy control group, deficiency 12(12.0%) versus 4(4.0%), and insufficient 72(72.0%) versus 46(46.0%) respectively. Rheumatological diseases in study patients were RA, osteoarthritis, osteoporosis, ankylosing spondylitis, SLE and other arthritis. Vitamin D level were lower in 100% SLE patients, 87.5% of osteoporosis, 83.33% of OA, 80% of RA, AS and other arthritis cases. The elderly population has been found to be a group of particular risk of vitamin D deficiency. This is in part due to them producing less cholecalciferol with the same exposure to UVB light as younger adults but also to less time spent outside<sup>19</sup> particularly true of those institutionalized elderly. Studies in both Turkey and Jordan showed that overall 59.9% of participants had a serum 25(OH)D level <30nmol/l (deficiency). Serum 25(OH)D was highest in women wearing western clothing and levels decreased to be lowest in traditional women wearing hijab and completely veiled women wearing niqab<sup>20</sup>. In our study, we found patients who had abnormal vitamin D level (deficient and insufficient) were more common in diseased group than healthy group (84; 84.0% vs 50; 50.0%) which was statistically significant ( $p$ -value<0.01) that reflected low serum vitamin D was associated with Rheumatological diseases. We also observed that low level of serum vitamin D was more common in subjects with inadequate exposure to sunlight in comparison to adequately exposed population in study patients (90.0% vs 80.0%) that reflects inadequacy of sun exposure negatively affects serum vitamin D level.

A number of recent studies have highlighted the association between SLE and vitamin D deficiency. In a study in 92 SLE patients (90% women, 98% white) it was found that 69 (75%) and 14 (15%) patients presented with vitamin D insufficiency and deficiency respectively<sup>21</sup>. Vitamin D deficiency is also more common in RA patients and may be one of the causes leading to development or worsening of the disease. In one study it was found that 84% patients of RA were vitamin D deficient versus only 34% of controls.<sup>14</sup> The serum vitamin D levels were also significantly lower in the RA patients (mean value of  $21.05 \pm 10.02$  ng/ml) as compared to the controls (mean value  $32.87 \pm 14.16$  ng/ml). There was a significant inverse correlation between serum vitamin D levels and RA disease activity. We also found similar results, vitamin D deficiency or insufficiency were in 100% cases of SLE patients and

80% patients of RA cases. Other Rheumatological diseased patients such as AS, osteoporosis, osteoarthritis, etc also had similar level of vitamin D.

## Conclusion

Vitamin D levels were lower in patients with Rheumatologic diseases than normal control group and female were more affected than male individuals. Life style also affected vitamin D status in patients with Rheumatologic diseases. Further large scale study is required pertinent to specific Rheumatologic disease to correlate effects of disease on vitamin D level and vice-versa.

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