

# Association of Vitamin D level with Disease Activity in SLE patients at a Tertiary Care Hospital

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## Abstract:

**Introduction:** Systemic lupus erythematosus (SLE) is a systemic autoimmune disease with increased prevalence in recent years. One of the extra skeletal functions of vitamin D is involved in regulation of immune response. **Objectives:** This study was to determine vitamin D status in SLE patients and the relationship with disease activity.

**Methods:** This prospective observational study was conducted at Medicine department in Dhaka Medical College and Hospital. Data regarding disease activity of SLE was taken from 50 SLE patients fulfilling ACR criteria and disease activity was calculated by SLEDAI score. Vitamin D level was quantified by ELISA.

**Results:** Out of 50 patients, 46(92%) were female and 4(8%) were male. Age range was 15 to 65 years and mean age was  $28.00 \pm 13.34$  SD. Most of the population reside in rural areas ( $n=32, 64\%$ ) and rest from urban areas ( $n=18, 36\%$ ). Common

presentations were fever (62%), proteinuria (50%), rash (40%), vasculitis (36%) and hematuria (34%). Overall mean SLEDAI score was  $18.24 \pm 9.67$ . Among the study population, 21(42%) patients had very highly active disease, 12(24%) patients had highly active disease, 11(22%) patients had moderately active disease and 6(12%) patients had mildly active disease. Mean vitamin D level was  $16.70 \pm 8.83$  ng/ml. In this study, majority were found to be vitamin D deficient 37(74%), out of rest 7(14%) patients had insufficient vitamin D level and 6(12%) patients had sufficient vitamin D. This study showed that there is negative linear correlation between SLEDAI score and vitamin D level which is statistically significant ( $p$  value  $< 0.001$  and  $r = -0.577$ ).

**Conclusion:** Low vitamin D level in SLE patients correlated with increased disease activity.

**Keywords:** (Systemic Lupus Erythematosus) SLE, SLE Disease Activity Index (SLEDAI), Vitamin D (Vit D).

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## Introduction:

SLE is a chronic multisystem inflammatory autoimmune disease characterized by immunological abnormalities resulting in production of auto antibodies. This autoimmune-mediated inflammation are stimulated by uptake of nucleic acid containing immune complexes by plasmacytoid dendritic cells and the resulting

activation of Type I interferon expression. This inflammatory milieu promotes defective function of regulatory T cells (Tregs) and hyperactivity of helper T cells (Th cells), and the survival and activation of auto reactive B cells that produce autoantibodies<sup>1</sup>. Evidence suggests that vitamin D impacts negatively on many of these events. This includes vitamin D-induced down regulation of the Th1 immune response and of the proliferation of activated B cells<sup>2</sup> while up regulating Tregs<sup>3</sup>. A recent study showed that vitamin D3 inhibits dendritic cell maturation and expression of IFN- $\alpha$  induced genes in SLE patients<sup>4</sup>. Vitamin D deficiency is highly prevalent in patients with SLE because of factors such as avoidance of sunshine due to photosensitivity<sup>5</sup>, the use of sun-screen<sup>6</sup>, chronic renal insufficiency<sup>7</sup> and the use of medications such as glucocorticoids<sup>8</sup>. Very few studies regarding level of vitamin D in patients with SLE has yet been conducted in Bangladesh. Therefore the data generated from the present study might be helpful to determine the level of vitamin D and to observe its association with disease activity in SLE patients.

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## Materials and Methods:

### Design of the Study

A prospective observational study was conducted at Medicine indoor of Dhaka Medical College Hospital. After getting approval from Dhaka Medical Ethical Review Committee, this study was done for six months of period, September 2016 to February, 2017 and patients suffering from SLE presenting to DMCH were recruited to participate in the study. Total 50 cases were enrolled and convenient sampling technique was used. All the SLE patients (based on ACR criteria) with or without getting treatment and who gave informed written consent were included in the study. Patients who have received vitamin D supplementation within previous 3 months were excluded. SLE patients with Chronic Kidney Disease, Chronic Liver Disease, Gastro-intestinal and Exfoliative skin disease were also excluded. A Pretested Structured Questionnaire Form was filled accordingly. After a detailed clinical examination and lab investigation, the clinical manifestations were categorized according to SLE Disease Activity Index (SLEDAI). It is a scoring system by which disease severity of SLE can be measured.

Mild activity (SLEDAI = 1-5)

Moderate activity (SLEDAI = 6-10)

High activity (SLEDAI = 11-19)

Very high activity (SLEDAI  $\geq 20$ )<sup>9</sup>.

Vitamin D (25(OH)D<sub>3</sub>) level was assessed using ELISA technique and categorized into 3 different levels:

Deficiency- 20 ng/ml or less

Insufficiency- 21 to 29 ng/ml

Sufficient - 30 ng/ml or more<sup>(10,11)</sup>.

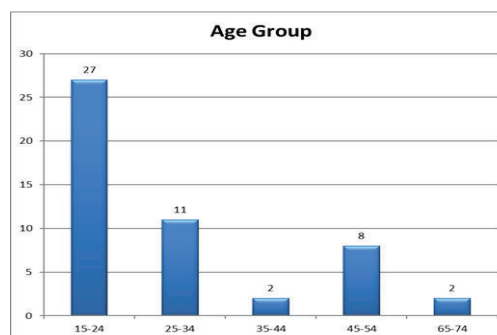
### Statistical Analysis

After editing and coding, the coded data directly entered into the computer by using SPSS 22 for WINDOWS RELEASE version. Data cleaning validation and analysis was performed using the SPSS/PC software, Graph and chart are by MS excel. Correlation between SLEDAI score and vitamin D level was analyzed by Pearson's Correlation test. Statistical significance was defined as p-value < 0.05.

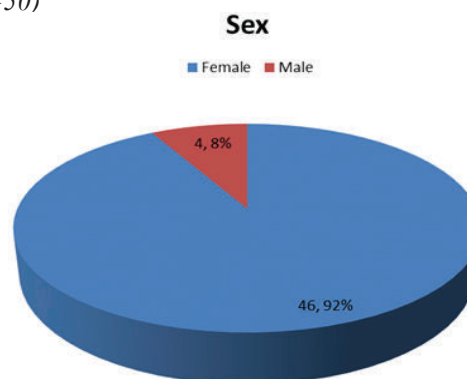
### Results:

Mean age was  $28.00 \pm 13.34$  with ranging from 15 to 65 years. 27 patients (54%) were of 15-24 years, 11 patients

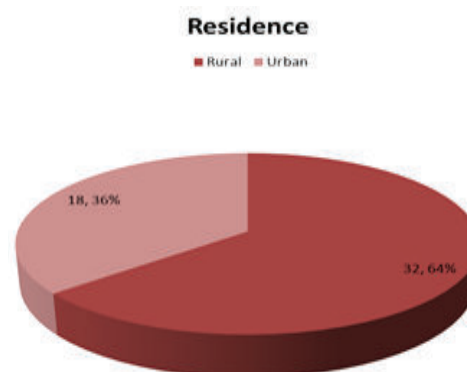
(22%) were 25-34 years, 8 patients (16%) were 45-54 years and 2 patients (4%) were from each of group 35-44 years and 65-74 years [figure 1]. There were 92% female SLE patients and 8% male SLE patients in this study [figure 2]. Among 50 cases majority came from rural area (32, 64%) and rest of patients were staying at urban area (18, 36%) (Figure 3). Most common presentation was fever (62%), followed by Increased DNA binding as determined by Farr assay (54%), proteinuria (50%), rash (40%), vasculitis (36%) and hematuria (34%) (Table I).



**Fig-1:** Distribution of patients in different age groups (n=50)



**Fig-2:** Sex distribution of patients (n=50)



**Fig-3:** Residence of patients (n=50)

**Table-I***Clinical manifestations of SLE patients (n=50)*

	Frequency	Percentage
Seizure	2	4 %
Visual disturbance	3	6 %
Lupus Headache	10	20 %
Vasculitis	18	36 %
Arthritis	4	8 %
Urinary Casts	5	10 %
Hematuria	17	34 %
Proteinuria	25	50 %
Pyuria	9	18 %
Rash	20	40 %
Alopecia	11	22 %
Mucosal Ulcers	8	16 %
Pleurisy	6	12 %
Pericarditis	2	4 %
Low Complement	26	52 %
Increased DNA binding	27	54 %
Fever	31	62 %
Thrombocytopenia	7	14 %
Leukopenia	2	4 %

Overall mean SLEDAI score was  $18.24 \pm 9.67$  and mean Vitamin D level was  $16.70 \pm 8.83$  SD ng/ml. Mean SLEDAI

was higher in female ( $17.12 \pm 8.94$ ) than that of male ( $11.80 \pm 6.35$ ). There was no significant difference in distribution. Mean Vitamin D level was also higher in female ( $17.12 \pm 8.94$ ) than male  $11.80 \pm 6.35$ , but the distribution across group was not significant either (Table II). In this study, 42% SLE patients had very highly active disease, 24% patients had highly active disease, 22% patients had moderately active disease and 12% patients had mildly active disease (figure 4). Majority were found to be vitamin D deficient (74%). 14% patients had insufficient vitamin D level and 12% patients were deficient in Vitamin D (figure 5).

Pearson's correlation co-efficient revealed a significant negative linear correlation between SLEDAI and vitamin D level. This means that SLEDAI decreased with increased vitamin D level in the blood (Figure 6).

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**Table-II***Mean, Standard deviation, maximum and minimum SLEDAI and vitamin D level (n=50)*

		Minimum	Maximum	Mean	Std. Deviation	P value*
SLEDAI	Female (n=46)	4	34	17.12	8.94	0.213
	Male (n=4)	23	26	11.80	6.35	
	Total (n=50)	4	34	18.24	9.67	
Vitamin D (ng/ml)	Female (n=46)	1.80	34.30	17.12	8.94	0.213
	Male (n=4)	6.30	17.30	11.80	6.35	
	Total (n=50)	1.8	34.3	16.70	8.84	

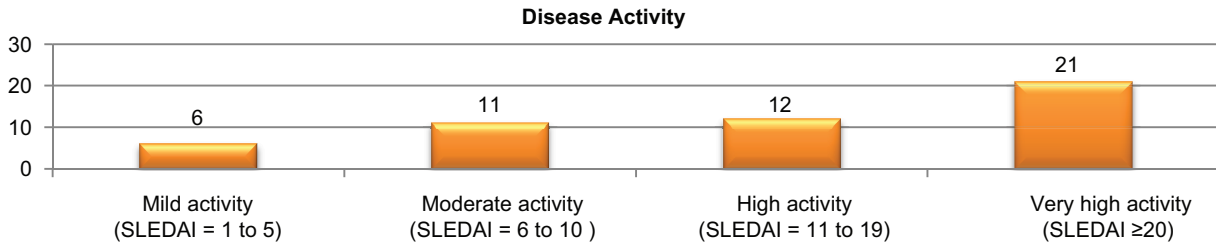


Fig.-4: Distribution of patents according to disease activity. (n=50)

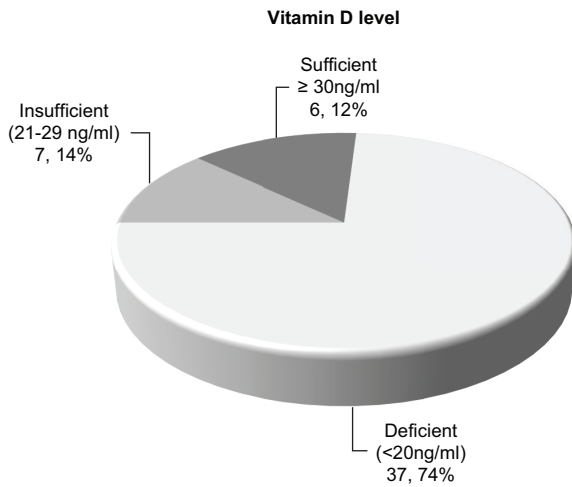


Fig.-5: Distribution of patients according to serum vitamin D level (n=50)

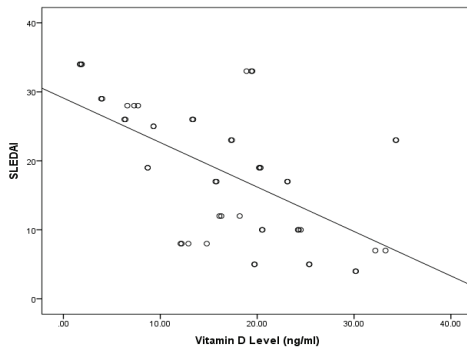


Fig.-6: Correlation between SLEDAI and Vitamin D level in blood

**Discussion:**

A total 50 SLE patients were studied and among the study population female are more prevalent. There were 92% female and 8% male. SLE is more common in females, where the reported female: male ratio is 8–15:1<sup>12</sup>. The findings of this study is also supported by study done

by Mandal M et al. and Nightingale Al et al<sup>[13,14]</sup>. Mean age was 28.00 ± 13.34 with ranging 15 to 65 years. SLE is a disease that can affect persons of all ages and ethnic groups and both sexes, but more than 90% of new patients presenting with SLE are women in the childbearing years<sup>15</sup>. Similar mean age (28.14 ± 8.43 SD) was found in a study by Mandal M et al [14]. Though slight difference (Mean age 31.12 ± 11.2 SD years) was found in study done by Handono K et al<sup>16</sup>. This difference could be the effect of different health seeking behavior pattern in different geographical variations.

In this study, most common presentation was fever (62%), followed by increased DNA binding as determined by Farr assay (54%), proteinuria (50%), rash (40%), vasculitis (36%) and hematuria (34%). In study of Bertias G et al. shows common pattern of clinical manifestation were photosensitivity rash(26%), malar rash (57%), discoid rash (11%), oral ulcer (59%), arthritis (60%), neuropsychiatric disease (9%), myocarditis (2%), serositis (5%), nephritis (37%) and vasculitis (13%). Arthritis was more common with advancing age (93% vs 72%, p<0.001), whereas renal disease (44% vs 33%, p=0.001), alopecia (47% vs 23%, p<0.001) and aphthous ulcerations (39% vs 26%, p=0.001) were more common in the young. Neuropsychiatric lupus was less common in mature-onset SLE (p<0.01). SLE was associated more commonly with thrombocytopenia (21% vs 15%, p=0.01), haemolytic anaemia (20% vs 3%, p<0.001). Leucopenia increased with advancing age (p<0.001)<sup>17</sup>.

This study showed mean Vitamin D level was 16.70 ng/ml. Mean Vit-D level was also higher in female (17.12 ± 8.94) than male 11.80 ± 6.35, but the distribution across group was not statistically significant (p value 0.213 > 0.05). This findings slightly lower the study done by Kalim H et al. He revealed that the mean of serum vitamin D level in his study was 22.80 ± 16.23 ng/ml. But

he could not examine the effect of sex difference with vitamin D level<sup>18</sup>.

In this study, majority were found to be vitamin D deficient (74%). 14% patients had insufficient vitamin D level and 12% patients were deficient in Vitamin. The findings is dissimilar with the study of Handono K et al. evidenced 55.56% with deficiency of vitamin D, 24.7% with insufficiency and 20.37% of SLE patients had normal vitamin D serum level [16]. Another study done by Kalim H et al. showed deficiency, insufficiency and normal level of vitamin D among SLE patients were 25.5%, 61.8% and 14.7% respectively<sup>18</sup>. This findings showed that low vitamin D level was frequent in SLE patients, and indicated that SLE patients had higher risk of insufficiency of vitamin D<sup>19</sup>. The high prevalence of SLE patients who have vitamin D level below normal was similar with other studies, with percentage between 50-75%, however those studies were performed in different latitude and ethnicity<sup>(20-22)</sup>.

According to the SLEDAI score, 42% SLE patients had very highly active disease, 24% patients had highly active disease, 22% patients had moderately active disease and 12% patients had mildly active disease. Overall, mean SLEDAI score of all study population was 18.24±9.67 SD. Mean SLEDAI was higher in female (17.12±8.94 SD) than male (11.80±6.35 SD). There was no significant difference of SLEDAI score among female and male (p value .213>.05). Moreover, Pearson's correlation co-efficient revealed a significant negative linear correlation between SLEDAI and vitamin D level. This means that SLEDAI decreased with increased vitamin D level in the blood and vice versa. Similar correlation is found in the study Handono K et al. [21] (p<.0000, r= -.659) and Mandal M et al. [13] (P<0.0001, r="0.42). A study performed by Sung in Korea showed that vitamin D did not correlate with disease activity<sup>21</sup>.

### Conclusion:

The mean vitamin D in SLE patients studied was low. The significant inverse relationship was found between serum vitamin D level and disease activity scores in SLE studied population. It indicates necessity for vitamin D supplementation in the management of SLE patients.

**Conflict of Interest:** All the authors do not have any conflict of interest in the subject matter or materials discussed in the manuscript.

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