Chest

The association between Vitamin D Deficiency and Pulmonary Affection in Rheumatoid Arthritis Patients

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ABSTRACT

Background: Rheumatoid arthritis (RA) is a systemic autoimmune disease causing symmetrical articular destruction with extraarticular manifestations that include pulmonary manifestations, which are major contributors to morbidity and mortality.

Aim of The Work: To detect the prevalence of vitamin D deficiency and its relationship to pulmonary affection in RA patients and correlate it with disease Activity .

Patients and Methods: The study is a cross sectional one, carried out on fifty patients with RA recruited from the Chest and Rheumatology Outpatient Clinics of Al Hussein University Hospital. All patients diagnosed with RA who fulfilled the American Colleague of Rheumatology/European League against Rheumatism 2010 classification criteria.

Results: In our study there was statistically significant (p-value = 0.002) increased DAS score in deficient patients (5.4 ± 0.8) when compared with insufficient patients (4.9 ± 0.4) and sufficient patients (4.1 ± 0.8). In our study there was statistically significant relation (p-value < 0.05) between vitamin D status and pulmonary manifestations (Exertional Dyspnea, Dry Cough, Chest Pain, Wheezing and Leathery Crepitation) which more frequent in deficient than insufficient and sufficient patients. In our study there was highly statistically significant (p-value < 0.001) decreased FVC in deficient patients (89.3 ± 20.1) when compared with insufficient patients (113.4 ± 7.1) and sufficient patients (114.8 ± 3.4). No statistically significant relation (p-value > 0.05) between vitamin D status and FEV1 & FEV1/FVC.

Conclusion: RA disease activity score (DAS-28 score) and pulmonary manifestations in RA patients were more prevalent in Vitamin D deficient than insufficient and sufficient patients.

Keywords: *Pulmonary; Rheumatoid arthritis; Vitamin D.*

INTRODUCTION

Rheumatoid arthritis (RA) is a systemic inflammatory disease that most typically affects the joints, producing progressive, symmetric, erosive destruction of cartilage and bone, and is often accompanied with autoantibody production. Extraarticular symptoms, such as pulmonary signs, are also linked to an increased risk of morbidity and mortality. They may even occur before articular symptoms. [1]

In rheumatoid arthritis, respiratory symptoms can be caused by a variety of conditions affecting the parenchyma, pleura, airways, or vasculature. Complications can occur as a result of rheumatoid arthritis or as a side effect of immune-suppressing medications used to treat rheumatoid arthritis. Within the first five years of disease, the bulk of respiratory signs arise. [2]

Vitamin D may have a significant impact on both the innate and adaptive immune systems. The presence of its receptors on several types of cells supports this, and its insufficiency is linked to the progression and result of RA. [3]

According to a 2012 Greek study published in Therapeutic Advances in Endocrinology and Metabolism, vitamin D insufficiency is closely linked to disabling symptoms in people with rheumatoid arthritis. This could be because RA can impair the body's ability to absorb vitamin D from the foods we eat, and low vitamin D levels can exacerbate RA symptoms and pain. [4]

Vitamin D reduces autoimmunity by modulating antigen-presenting cells' synthesis of pro-inflammatory and anti-inflammatory cytokines. A decrease in 25(OH) D3 is caused by polymorphisms in the vitamin D receptor and 1-hydroxylase genes, which may increase the risk of inflammation.[5]

The aim of the study to detect the prevalence of vitamin D deficiency and its relationship to pulmonary affection in RA patients and correlate it with disease Activity.

PATIENTS AND METHODS

The study was a cross sectional one, carried out on 50 patients diagnosed with RA recruited from the Chest and Rheumatology Outpatient Clinics of Al Hussein University Hospital in period between August 2021 and May 2022.

Ethical Considerations: The selection of subjects done after prior explanation of the aim of the study, and a free-will written approval consent is taken, and the whole work done according to the ethical committee, Faculty of medicine, Al-Azhar University

Inclusion criteria include: All patients diagnosed with RA who fulfilled the American Colleague of Rheumatology/European League against Rheumatism 2010 classification criteria.

Exclusion criteria include: No specific contraindications.

All studied patients are subjected to: Detailed history taking. Physical examinations, Laboratory investigations were performed including complete blood count, erythrocyte sedimentation rate (ESR), C-reactive protein titer, liver enzymes, and renal function tests. Rheumatoid factor (RF) titer was determined using the latex agglutination test kit and anti-CCP antibody titer using the ELISA technique, serum 25-hydroxy vitamin D [25(OH) D] levels was performed using ELISA, Chest x-ray, High Resolution Computed Tomography(HRCT) Chest, and Spirometry   Statistical analysis:The Statistical Program for Social Science (SPSS) version 24 was used to examine the data. The mean and standard deviation were used to express quantitative data. Frequency and percentage were used to express qualitative data. The central value of a discrete set of numbers, namely the sum of values divided by the number of values, is called the mean (average). The standard deviation (SD) is a measure of a set of values' dispersion. A low SD implies that the values are spread out over a wider range, whereas a high SD shows that the values are close to the set's mean. When comparing non-parametric data, the Chi-square test was utilized. To compare quantitative data on vitamin D levels, the Kruskal Willis test was utilized. For data correlation, the Pearson correlation coefficient was applied. P-values less than 0.05 were considered significant, P-values less than 0.001 were regarded very significant, and P-values more than 0.05 were considered inconsequential.

RESULTS

		Studied patients (N = 50)	
Age (years)	M±SD	46.7 ± 6.6	
	Min – Max	38 – 61	
Duration of RA disease (years)	M ±SD	13.9 ± 5.6	
	Min – Max	1 – 23	
Sex	Male	10	20%
	Female	40	80%
Smoking	Non-smoker	45	90%
	Smoker	5	10%

Table 1: Description of demographic data in all studied patients

The result of our study showed that the description of demographic data in all RA patients with pulmonary affection shown that the mean age of all studied patients was 46.7 ± 6.6 years with minimum age of 38 years and maximum age of 61 years. As regard duration, the mean duration of all studied patients was 13.9 ± 5.6 years with minimum duration of 1 year and maximum duration of 23 years. As regard sex, there were 10 males (20%) and 40 females (80%) in the studied patients. As regard smoking, there were 5 smokers (10%) and 45 non-smokers (90%) in the studied patients. Table (1)

Vitamin D level	Studied patients (N = 50)	
Deficient (<20 ng/ml)	22	44%
Insufficient (20 – 30 ng/ml)	22	44%
Sufficient (>30 ng/ml)	6	12%

Table 2: Vitamin D serum level in all studied patients.

In our study, the description of vitamin D status in all studied patients were 22 deficient patients (44%), 22 insufficient patients (44%) and 6 sufficient patients. Table (2)

		Studied patients (N = 50)	
CT findings	Normal CT	0	0%
	Bronchiectasis	30	60%
	Honey combing	13	26%
	Emphysema	20	40%
	Reticulations	32	64%
	Pleural effusion	5	10%
	pleural thickening	15	30%
	Nodule	5	10%
	GGO	27	54%
	Sub-pleural cysts	2	4%
CT pattern of ILD	NSIP	24	48%
	UIP	17	34%
	RB-ILD	9	18%

Table 3: Description of CT chest findings in all studied patients

As regard CT pattern of interstitial lung affection, the most common pattern was NSIP in 24 patients (48%), UIP in 17 patients (34%) and RB-ILD in 9 patients (18%). Table (3)

		Vitamin D status			Stat. test	P-value
		Deficient (n = 22)	Insufficient (n = 22)	Sufficient (n = 6)		
DAS-28 score	Mean	5.4	4.9	4.1	KW	= 0.002 S
	±SD	0.8	0.4	0.8	12.7	

Table 4: The correlation between vitamin D level and DAS- 28 score

DAS-28 (disease activity score) and 28 mention to the count of peripheral joints examined for tenderness in rheumatoid arthritis patient

In all patients, A relationship is present between vitamin D level and DAS-28 in Vit-d deficient patients, study found a significant (p-value = 0.002) rise in DAS-28 score.(5.4 ± 0.8) when compared with insufficient patients (4.9 ± 0.4) and sufficient patients (4.1 ± 0.8). Table (4)

		Vitamin D status						X^2	P-value
		Deficient (n = 22)		Insufficient (n = 22)		Sufficient (n = 6)			
Exertional Dyspnea	No	14	63.6%	14	63.6%	6	100%	3.2	0.201 NS
	Yes	8	36.4%	8	36.4%	0	0%		
Dry Cough	No	14	63.6%	14	63.6%	5	83.3%	0.9	0.634 NS
	Yes	8	36.4%	8	36.4%	1	16.7%		
Chest Pain	No	20	90.9%	20	90.9%	4	66.7%	2.9	0.230 NS
	Yes	2	9.1%	2	9.1%	2	33.3%		
Wheezing	No	18	81.8%	21	95.5%	5	83.3%	2.1	0.354 NS
	Yes	4	18.2%	1	4.5%	1	16.7%		
Leathery Crepitation	No	17	77.3%	17	77.3%	6	100%	1.7	0.426 NS
	Yes	5	22.7%	5	22.7%	0	0%		

Table 5: Relation between vitamin D status and clinical manifestations in all studied patients

In our study there no statistically significant relation (p-value < 0.05) between vitamin D status and clinical manifestations (Exertional Dyspnea, Dry Cough, Chest Pain, Wheezing and Leathery Crepitation). Table (5)

		Vitamin D status			KW	P-value
		Deficient (n = 22)	Insufficient (n = 22)	Sufficient (n = 6)		
FVC	Mean	89.3	113.4	114.8	16.6	< 0.001 HS
	±SD	20.1	7.1	3.4		
FEV1	Mean	80.1	84.8	86.0	4.36	0.113 NS
	±SD	8.4	4.7	5.0		
FEV1/FVC	Mean	89.9	74.7	74.5	3.8	0.144 NS
	±SD	22.0	4.2	3.3		

Table 6: Relation between vitamin D status and Spirometric indices in all studied patients

There is significant decrease in FVC (p-value < 0.001) in Vit-D deficient patients (89.3 ± 20.1) when compared with insufficient patients (113.4 ± 7.1) and sufficient patients (114.8 ± 3.4). No significant difference (p-value > 0.05) in vitamin D status and FEV1 & FEV1/FVC. Table (6)

		Vitamin D status						X^2	P-value
		Deficient (n = 22)		Insufficient (n = 22)		Sufficient (n = 6)			
PFTs pattern	Small airway disease	1	4.5%	7	31.8%	3	50%	29.8	0.001 S
	Mild restrictive	7	31.8%	0	0%	3	50%		
	Moderate restrictive	6	27.3%	5	22.7%	0	0%		
	severe restrictive	5	22.7%	0	0%	0	0%		
	Mild obstructive	0	0%	3	13.6%	0	0%		
	Mixed	3	13.6%	7	31.8%	0	0%		

Table 7: Relation between vitamin D status and PFTs pattern in all studied patients

The study shows that there was statistically significant difference between vitamin D deficient patients, insufficient patients, and sufficient patients as regard PFTs pattern. Table (7)

		Vitamin D status						X^2	P-value
		Deficient (n = 22)		Insufficient (n = 22)		Sufficient (n = 6)			
Bronchiectasis	No	0	0%	14	63.6%	6	100%	28.8	< 0.001 HS
	Yes	22	100%	8	36.4%	0	0%		
Honey combing	No	10	45.5%	21	95.5%	6	100%	16.7	< 0.001 HS
	Yes	12	54.5%	1	4.5%	0	0%		
Emphysema	No	2	9.1%	22	100%	6	100%	42.4	< 0.001 HS
	Yes	20	90.9%	0	0%	0	0%		
Reticulations	No	10	45.5%	6	27.3%	2	33.3%	1.59	0.449 NS
	Yes	12	54.5%	16	72.7%	4	66.7%		

Pleural Effusion	No	19	86.4%	20	90.9%	6	100%	1.01	0.603 NS
	Yes	3	13.6%	2	9.1%	0	0%		
pleural thickening	No	16	72.7%	16	72.7%	3	50%	1.29	0.522 NS
	Yes	6	27.3%	6	27.3%	3	50%		
Sub-pleural cysts	No	18	81.8%	21	95.5%	6	100%	3.03	0.220 NS
	Yes	4	18.2%	1	4.5%	0	0%		
Nodule	No	10	45.5%	7	31.8%	6	100%	8.8	0.012 S
	Yes	12	54.5%	15	68.2%	0	0%		
GGO	No	22	100%	20	90.9%	6	100%	2.6	0.266 NS
	Yes	0	0%	2	9.1%	0	0%		

Table 8: Relation between vitamin D status and CT findings in all studied patients

In our study there was no significant difference between vitamin D status and the following CT findings (reticulations, pleural effusion, pleural thickening, sub-pleural cysts and GGO). Statistically significant (p-value = 0.012) increased percentage of nodule in deficient patients (12 patients, 54.5%) and insufficient patients (15 patients, 68.2%) when compared with sufficient patients (0 patients, 0%). Highly statistical significant (p-value < 0.001) increased percentage of emphysema in deficient patients (12 patients, 54.5%) when compared with insufficient patients (0 patients, 0%) and sufficient patients (0 patients, 0%). Highly statistical significant (p-value < 0.001) increased percentage of honey combing in deficient patients (12 patients, 54.5%) when compared with insufficient patients (1 patient, 4.5%) and sufficient patients (0 patients, 0%). Highly statistical significant (p-value < 0.001) increased percentage of Bronchiectasis in deficient patients (22 patients, 100%) when compared with insufficient patients (8 patients, 36.4%) and sufficient patients (0 patients, 0%). Table (8)

DISCUSSION

The association between RA and serum levels of vit D and 1,25(O.H)2D has been controversial in previous studies.[6]

A large meta-analysis study carried out by Lin et al. [4] that included 3489 patients showed that RA patients had lower vitamin D levels than the healthy controls.

Other research, on the other hand, found no such link. Differences in prior studies' results could be due to a variety of factors, including the population investigated, sample size, study design, analytical procedures utilized, and testing tools. 6 to 1

Abourazzak et al.[7] discovered vitamin D deficiency in 64.4 (0.9 percent) and insufficiency in 35.5 and 99.1 percent of their RA patients, respectively.

Vitamin D and IPF have a statistically significant inverse relationship, according to Allam et al. (r=0.234, P=0.017). [3]

In a previous study of 67 patients with ILD secondary to connective tissue disease including RA and 51 patients with other causes of ILD, significant vitamin D deficiency (52 vs. 20%,P<0.0001) and insufficiency (79 vs. 31%, P<0.0001) were found among those with connective tissue disease-ILD than those with other forms of ILD.[2]

Our study agrees with that done by Sherin et al.[8] which showed an association between pulmonary affection in RA patients and hypovitaminosis D as in RA patients with pulmonary affection 45% of patients have vitamin D deficit and 45% had vitamin D insufficiency versus 16.7 and 63.3% in RA patients without pulmonary affection.

The description of CT results in all studied patients. As regard CT findings, there was bronchiectasis in 30 patients (60%), honey combing in 13 patients (26%), emphysema in 20 patients (40%), reticulations in 32 patients (64%), pleural effusion in 5 patients (10%), pleural thickening in 15 patients (30%), nodule in 5 patients (10%), GGO in 27 patients (54%) and sub-pleural cyst in 2 patients (4%).

Our study agrees with that done by Haque U et al.[9], Sherin et al.[8] andTurhanoflu AD et al.[10]which showed that there were inverse associations between vitamin D level with RA disease activity (DAS-28 score).

A meta-analysis by Lin et al.,[4]reported the same association and reported a relatively stronger negative correlation between 25(OH)D and DAS-28 in low latitude areas and in developing countries than in developed countries.

This result agrees with that done by Sherin et al.[8]abnormal spirometric parameters were more among the deficient and insufficient groups than the sufficient group, P=0.01, and the most common pattern among the vitamin D deficiency and insufficient groups was the restrictive pattern in 21.4% in both groups. Significant decrease in DLCO level in deficient group more than insufficient and sufficient groups (P=0.03).

In contrary with the study done by Sherin et al.[8]the 40 RA patients with pulmonary affection as diagnosed by HRCT chest, a ground glass appearance was found in 22 (55%) RA patients, pleural thickening in 12 (30%) patients reticulation in 26 (65%) patients, honey combing in 10 (25%) patients, nodules in four (10%) patients, emphysema in 16 (40%) patients,bronchiectasis in 24 (60%) patients, and pleural effusion in four (10%) patients

CONCLUSION

Vitamin D insufficiency appears to be very common among RA patients., This study suggests that pulmonary manifestations in RA patients more prevalent with vitamin D deficiency, This study suggests that vitamin D is associated with RA disease activity, and may have a role in functional disability in RA patients.

Conflict of interest : none

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