

# The Association between Depression and vitamin D level with disease activity in patient with rheumatoid arthritis

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## Original Article

### Abstract

**Introduction:** Rheumatoid arthritis (RA) is a chronic rheumatologic disease, affecting different aspects of patient life. Although several studies have reported a higher rate of depression among patients with RA, there is still controversy over the underlying risk factors and probable covariates of depression in these individuals. The present study investigated the relationship between disease activity, serum levels of vitamin D, and depression in patients with RA.

**Methods:** In this cross sectional study patients with confirmed RA based on the American College of Rheumatology guidelines entered the study. Disease activity was measured using the Disease Activity Score (DAS). The Hospital Anxiety and Depression Scale (HADS) was also administered to determine the subjects' level of depression. The Health Assessment Questionnaire (HAQ) was applied for evaluating the subjective disability of the patients in their daily activities. Serum levels of vitamin D, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR) were also measured.

**Results:** 62 patients were enrolled in the study. Depression was present and possibly present in 12 (19.4%) and 15 (24.2%) cases, respectively. According to the results the DAS was inversely associated with vitamin D3 levels ( $P < 0.001$ ). There were also significant relations between the DAS and scores on both the HAQ and HADS. Moreover, higher levels of vitamin D3 were related with lower scores on the HAQ and HADS ( $P = 0.018$ ).

**Conclusion:** Higher scores on the HADS were directly associated with lower levels of vitamin D, HAQ score and disease activity. Nevertheless, no significant association was found with HADS and patients' sociodemographic characteristics. Targeted approach to psychological aspects and vitamin D levels among patients with RA may have considerable implication for the optimal management of RA.

**Key words:** Rheumatoid Arthritis, Depression; Vitamin D

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## Introduction:

Rheumatoid arthritis (RA) is one of the most debilitating illnesses worldwide affecting 1% of population. This disease is characterized with its chronic course, unpredictable flares with extreme pain and disability (1). The progressive nature of the illness and the consequent dependence of the patients on their caregivers impose considerable psychological burden on patients with RA. Such unceasing unpleasant circumstances would not only disturb the patients' coping mechanisms and psychological balance, but also make them more vulnerable to psychosocial issues and suicidal ideation (2).

Several studies have suggested a higher rate of depression in patients with RA than other illnesses such as osteoarthritis and in the general population (3,4). The prevalence according to different measuring methods has a wide range of 3-40% (5).

It has been reported 14.8% (when used with the Hospital Anxiety and Depression Scale (HADS) (6). Moreover, Risk of mortality is increased in patients with RA (7,8). Researchers have hence sought to identify the probable risk factors and covariates of the occurrence of depression in this group of patients. Several factors including low socioeconomic status, gender, age, functional limitation, pain and systemic inflammation have been related to depression among persons with RA (9). While some studies have confirmed associations between depression and the course, disease activity, clinical symptoms of the illness, as well as several psychosocial and demographic factors in people with RA (10-12), others have introduced the socioeconomic status of the patients, rather than the clinical features or activity of RA, to be linked with depression (13,14). Besides, there is conflicting data regarding association of vitamin D and depression (15,16). On the other hand, vitamin D is associated with disease activity in patients with RA (17).

Therefore, the present study is aimed to estimate the prevalence of depression among patients with RA. It also attempted to investigate the possible associations between depression and disease activity, general health, serum vitamin D levels, and acute phase reactants in these patients.

## Methods:

### Patients and Procedures:

In this cross sectional study a total of 62 individuals with confirmed diagnosis of RA based on the American College of Rheumatology (ACR) classification criteria (18) who presented at the Rheumatology Clinic of Rasoul-e-Akram Hospital (Tehran, Iran) during January 2011- March 2013 were randomly recruited. This study was approved by the Ethics Committee of Affiliated medical university. Written informed consent was obtained from all patients. Subjects with a known history of depression before the onset of RA, or a history of other chronic and debilitating illnesses, as well as other rheumatologic conditions including fibromyalgia, were excluded and replaced. Likewise, patients who had received oral/parenteral vitamin D supplements over the past three months or taking anti depressant medications were also excluded.

### Measurement Instruments:

We used Liston device, Cal biotech kit and ELIZA method to measure vitamin D level. Demographic data (age, gender, marital status, and economic condition), along with disease duration and the prescribed drugs, were collected from the patients' hospital file and recorded in a checklist.

The previously validated in Persian of Hospital Anxiety and Depression Scale (HADS) was used to assess the patients' levels of depression and anxiety. HADS, measured depression on a linear scale, i.e. higher scores indicate greater level of anxiety and depression. The scale contains seven items on depression which are scored on a four-point scale (from 0 to 3). The normal range for the total scores of depression, (obtained by summing the scores of all seven items), is 0-7. Scores 8-10 and 11-21 suggest the probable presence and presence of depression, respectively (19-21).

The patients' subjective disability in daily activities was measured using Iranian validated form of the self-administered Health Assessment Questionnaire (HAQ). The HAQ asks the patients to evaluate their ability to do certain daily tasks, including eating, walking, arising, dressing and grooming, as well as their independence in hygiene, reaching, gripping and opening things, and errands and chores (22-24).

Vitamin D3 levels, quantitative levels of erythrocyte sedimentation rate (ESR), semi-quantitative amounts of C-reactive protein (CRP) were then measured in the sera of patients.

The Disease Activity Score (DAS) was applied to assess the disease activity. This score is considered to be the most specific tool to measure inflammation in RA and represents an absolute number in each setting and for each patient. The DAS consists of four distinguished components, namely swollen joint count, tender joint count, ESR or CRP, and global estimate of patient health (25).

Data were entered into a commercially available biostatistical software package (the last version of SPSS) and then analyzed. Independent t-tests and Chi 2 were used to compare the mean scores of groups. P-values less than 0.05 were considered significant.

## Results:

Overall, 62 patients, including nine men (14.5%) and 53 women (85.5%), entered the study. The mean age of the patients and the mean duration of the disease were 48.4 years and 87.4 months (range: 2-384 months), respectively. Six patients (9.7%) were illiterate, 25 (40.3%) didn't finish high school, 22 (35.5%) were high school graduates, and nine (14.5%) held a college degree.

Low, moderate, and adequate levels of income were reported by 26 (41.9%), 30 (48.4%), and six (9.7%) individuals, respectively (Table 1).

Table 1. Demographic data of patients

Variable	Frequency (%) or Mean (SD)
Age (year)	48.4 (14.1)
Gender (male)	9 (14.5%)
Disease duration (month)	87.8 ( 84.9)
Educational level	
Illiterate	6 (9.7%)
High school	25 (40.3%)
High school graduated	22 (35.5)
College degree	9 (14.5%)
Income level	
Low	26 (41.9%)
Moderate	30 (48.4%)
Sufficient	6 (9.7%)

The participants' mean serum ESR level was 22.6. CRP was negative in 37 subjects (59.7%) and positive in the remaining 25 (40.3%).

Depression was found to be possibly present and present in 15 (24.2%) and 12 (19.4%) patients, respectively. 30 individuals (35%) had normal scores on the HADS (no depression), (Figure 1).

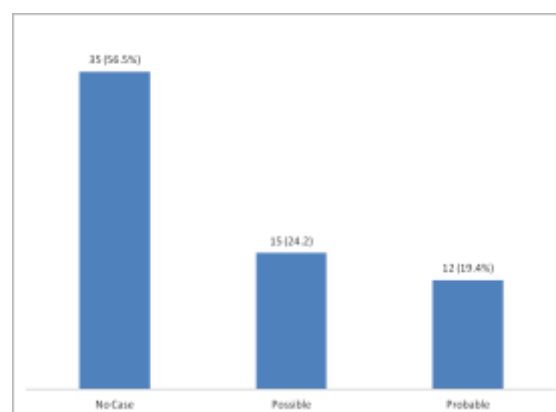


Figure 1. Stratifying the patients based on the HAD score. No case: no case of depression; Possible: possible case of depression, Probable case: probable case of depression

Table 2. Maximum, minimum, mean and standard deviation of the scores of the applied measures

Measures	DAS	HAQ	HAD
Maximum score	8.46	20	16
Minimum score	0.97	0	3
Mean±SD	3.3±1.5	606±5.2	7.2±3.3

SD: Standard Deviation

Table 2 summarizes the scores of the patients on DAS, HAQ, and HADS. There was a significant inverse relationship between the DAS and vitamin D3 levels ( $P < 0.001$ ). The DAS was also significantly related with the HAQ and HADS scores ( $P = 0.001$  and  $0.009$ , respectively).

Moreover, higher levels of vitamin D3 were associated with lower scores on the HAQ ( $P = 0.018$ ). According to the DAS, the inflammation level was high in eight patients (12.9%), moderate in 24 patients (38.7%), and low in 30 patients (48.4%) (Figure 2). No statistically significant relations were detected between the subjects' socio-economic and educational characteristics and their scores on different scales.

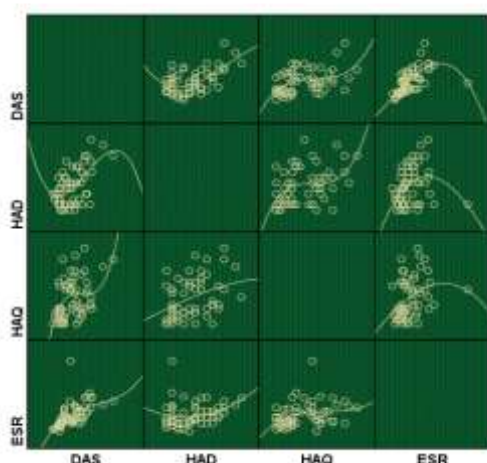


Figure 2. Association of HAD, HAQ, DAS, ESR, CRP

### Conclusion:

As a chronic debilitating disease, RA affects the patients' quality of life and steals their potentially fruitful years of lifespan. Coexistence of depression and RA can increase the suffering of these patients.

Studies have demonstrated that depressed patients with RA perceive more pain and feel more debilitated in comparison to non-depressed patients with identical disease activity (11-13). It is also believed that depression decreases the patients' adherence to the treatment (14).

Although several studies have report a higher rate of depression among patients with RA in comparison with the general population (4-8), a 10-year longitudinal study on 6153 patients did not show higher scores on depression measures or more common depressive symptoms in patients with RA compared to those with other clinical conditions (15). However, depression was either present, or likely to be present in 43.6% of our participants.

A systematic review and meta-analysis estimated the prevalence of major depressive disorder in Iran at 4.1% (26). Despite the administration of different measures in different studies, depression seems to be much more prevalent in patients with RA than in the general population. As HADS spares somatic features of depression, it is considered to report less false positives than similar questionnaires.

Research on risk factors of depression in patients with RA has yielded contrasting results.

According to our study depression was not associated with sex, marital status, educational and income level. However was independently related to DAS. Fuller et al reported that depression was more frequent in female, younger and poorer patients (3). Mella on study compared RA with osteoarthritis patients found HADS was related to lower education and higher disease activity (5). In contrast Hawley et al was declared that depression was related to socioeconomic not clinical factors and disease activity (16). Different depression measures may be one of the cause varieties in literature (4).

Lower levels of vitamin D were also associated with higher scores on the HADS and the DAS. Some evidences investigate association of the role of vitamin D with depression (18,19,31).

In a study on 1000 elderly subjects, the mean levels of vitamin D were significantly lower in patients suffering from major or minor depression compared to their control counterparts (27).

In another study on 75 patients with fibromyalgia, vitamin D deficiency was more common in patients with both fibromyalgia and depression (28).

A study on 850 patients with RA suggested independent relationships between vitamin D deficiency and both highly sensitive CRP and tender joint counts (29). However, it is still unclear whether vitamin D independently increases the risk of depression in RA patients or affects the psychological features of patient life by aggravating the course of their illness. If depression and vitamin D are component of DAS as well as vitamin D has been linked with depression, pharmacological approach of depression and low vitamin D level for optimal RA treatment is justified. Further research is required to clarify such issues.

This study has several limitations, first our survey was cross sectional with limited patients, and longitudinal prospective study with sophisticated number of participant would be more useful. Second, economic status was based on patients' report, it would be better to measure standard economic family status.

This study showed independent correlation with vitamin D level, HADS, HAQ and DAS which may entail targeted focus on treatment of depression

and low vitamin levels for achieving better RA outcome.

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## ارتباط افسردگی با سطح ویتامین D و شدت بیماری در بیماران مبتلا به آرتریت روماتوئید

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### چکیده

**مقدمه:** آرتریت روماتوئید بیماری روماتیسمی مزمنی است که بر جنبه‌های مختلف زندگی افراد اثر می‌گذارد. اگرچه مطالعات متعددی شیوع بالای افسردگی در مبتلایان به این بیماری را گزارش کرده است ولی هنوز اتفاق نظر در مورد فاکتورهای خطر و متغیرهای افسردگی در این بیماران وجود ندارد. مطالعه اخیر ارتباط بین شدت بیماری، سطح سرمی ویتامین D و افسردگی در بیماران مبتلا به آرتریت روماتوئید را مورد بررسی قرار داده است.

**روش کار:** در این مطالعه مقطعی، بیماران با تشخیص قطعی آرتریت روماتوئید بر اساس معیارهای انجمن روماتولوژی آمریکا وارد شدند. سطح فعالیت بیماری با معیار ((DAS)) مورد ارزیابی قرار گرفته شد. در مورد امتیازبندی افسردگی از معیار ((HADS)) استفاده شده است. میزان ناتوانی بیماران در انجام فعالیت‌های روزانه با پرسشنامه HAQ ارزیابی شد. سطح سرمی ویتامین D و ESR و CRP نیز اندازه‌گیری شد.

**نتایج:** ۶۲ بیمار در این مطالعه وارد شدند. بر اساس HADS score ۳۰ بیمار (۳۵ درصد) افسرده نبودند. البته افسردگی قطعی و احتمالی به ترتیب در ۱۲ بیمار (۱۹/۴ درصد) و ۱۵ بیمار (۲۴/۲ درصد) وجود داشت. بر اساس نتایج بدست آمده، ارتباط معنی‌داری بین معیار DAS با HAQ و HADS وجود داشت ( $P=0/001$  و  $P=0/009$  به ترتیب). علاوه بر این سطوح بالاتر ویتامین D با امتیاز پایین‌تر در معیارهای HAQ و HADS همراه بود ( $P: 0/018$ ).

**نتیجه‌گیری:** سطوح بالای امتیاز HADS مستقیماً با سطوح پایین‌تر ویتامین D و HAQ پایین‌تر و فعالیت بالاتر بیماری مرتبط است. هیچ ارتباطی بین امتیاز HADS با ویژگی‌های اجتماعی بیماران وجود نداشت. توجه ویژه به وضعیت روحی روانی بیماران و سطح ویتامین D می‌تواند تأثیر به‌سزایی در درمان مبتلایان به آرتریت روماتوئید داشته باشد.

**کلیدواژه‌ها:** ویتامین D، آرتریت روماتوئید، افسردگی

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