

Prevalence of Depression among Hospital Based Rheumatoid Arthritis Population and its Associated Factors

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Citation: Shoukry HS (2021) Prevalence of Depression among Hospital Based Rheumatoid Arthritis Population and its Associated Factors. Arch Med Vol.13 No.2:6

Abstract

Background: Depression is of high prevalence among rheumatoid arthritis patients compromising the physical and psychological aspects of quality of life. It is highly associated with VIT D level.

Patients and methods: This study included 200 RA patients. (BDI) was used to detect depression. Disease activity was measured using disease activity score (DAS-28) and Rheumatoid Arthritis Disease Activity Index (RADAI-5). The Modified Health Assessment Questionnaire (MHAQ) was used for measuring disability. Rheumatoid Arthritis Quality of Life scale (RAQoL), Visual Analogue Score-pain (VAS-pain), and Fatigue Severity Scale (FSS) scores were calculated.

Results: The mean disease duration 6.75 ± 4.32 years, 69.5% were females and 30.5% males (F: M 2.27:1). Their mean DAS-28 was 3.97 ± 1.19 and MHAQ 1.27 ± 0.63 . The mean BDI II score was 21 ± 12.61 . 48.5% of the patients had moderate depression 4.5% had severe depression. BDI II significantly correlated with erythrocyte sedimentation rate, C-reactive protein, DAS-28, MHAQ, RAQoL VAS-pain FSS and RADAI ($p=0.001$).

Conclusion: Depression is highly prevalent among rheumatoid arthritis patients. Screening for depression periodically in RA should be included management protocols to avoid poor outcomes.

Keywords: Depression; Rheumatoid arthritis; Beck depression inventory

Abbreviations: ESR: Erythrocyte Sedimentation Rate; CPR: C Reactive Protein; DAS-28: Disease Activity Score; MHAQ: The Modified Health Assessment Questionnaire; RAQoL: Rheumatoid Arthritis Quality of Life; VAS: Visual Analogue Scale; FSS: Fatigue Severity Scale; RADAI-5: Rheumatoid Arthritis Disease Activity Index

Received: December 30, 2020; **Accepted:** January 29, 2021; **Published:** February 05, 2021

Introduction

Rheumatoid Arthritis (RA) is a severe chronic progressive inflammatory autoimmune disorder of unknown etiology [1,2]. Genetic and environmental causes are believed to have a role, as in the case of other autoimmune diseases [3]. The disease is characterized by systemic inflammation where the connective tissues (cartilage and joint synovium) are most frequently targeted and affected [4]. It is associated with personal cost and challenge, due to the increasing prevalence, chronic periodicity

with acute exacerbations, functional impairment and progressive disability [1].

For almost a century it has been observed that there is an epidemiological link and associations between RA and psychological problems [5]. Patients with RA have a high prevalence of depression comorbidity. The lifetime prevalence of depression in RA patients was reported to be 41-66% [6-8]. A Canadian study reported that the prevalence of depression was 46% higher in patients with RA compared to a matched control group [9].

The factors that contribute to depression in rheumatic patients are diverse. It is not clear whether the mechanism of psychiatric comorbidity related to the immune-inflammatory state or it is a sequel of the chronic illness and disability [10]. The disease activity with long term pain [11], suffering from somatic symptoms [12,13] functional limitations [14] and disease progression may contribute to depression development [12].

Psychiatric disorders have been identified as major causes of disease burden and disability [15]. They can worsen Health-Related Quality Of Life (HRQoL) [15], compromise medical treatment, management [15] and leading to high costs of health care services [16]. Moreover RA patients with comorbid depression were shown to have increased levels of pain, irrespective the disease activity [17] and expanded mortality rates [18,19]. Comorbid depression is an independent risk factor for cardiovascular disease as myocardial infarction [20] and increase overall mortality [21]. Several studies suggested that depression may also be important determinants of work impairment [22]. In RA, depression has been found to predict future disability pension [23] and functional disability [24].

Despite the associated adverse outcomes that occurred there is no optimal management of comorbid depression in rheumatic patients. It is not fully characterized in the medical literature or prioritized in major treatment guidelines. It is not appropriately recognized and managed by all healthcare providers [25-27]. The studies that estimate the prevalence of comorbid depression received less attention in medical literature [28,29].

The aim of the study to was determine the prevalence of depression among patients with rheumatoid arthritis and its relationship with socio demographic factors and disease activity measuring parameters.

Patients and Methods

This cross section analytical study was conducted at the clinical rheumatology and immunology department at Kasr-Alainy hospital, Egypt. Data was collected starting from February 2018 till December 2019. A total of 200 patients fulfilling the American College of Rheumatology/European League against Rheumatism (ACR/EULAR) 2010 classification criteria for Rheumatoid arthritis diagnosis [30]. The mean duration of the disease among participants was 6.75 years. The diagnosis was determined after detailed reviewing of the patients' complete medical records and discussing the case with their resident doctors.

All the patients were above 18 years old. The patients excluded from the study were A) Patients with CNS lupus, psycho-organic syndrome or cognitive impairment B) Patients who were receiving daily dose of prednisolone more than 10 mg, because of the potential impact on Beck Depression Inventory (BDI) results. C) Patients having any chronic disease beside rheumatoid arthritis. Moreover, C) Patients with disease duration was shorter than one month, because the reaction to diagnosis report can increase BDI scores. Also, patients who were not willing to write consent were excluded.

Sampling

Non probability sampling was done were all admitted patients during the study period fulfilling the inclusion criteria were included in the study.

Data collection tools

1. Questionnaire consisting of the socio demographic characteristics of the patients age (years), Gender, Education, working status, Residency and Marital status. It included also clinical data of the disease such as medical history, age of disease onset number of tender and swollen joints.
2. Assessment of depression among patients with autoimmune diseases was done through interviewing the patients using Beck Depression Inventory (BDI) questionnaire version II (BDI II). It is one of the most widely used psychometric tests for measuring the presence and severity of depression. It consists of 21 items (questions) presented in multiple-choice format. BDI evaluates symptoms of depression, fifteen items express emotions, four cover behavioural changes, and six concerns somatic symptoms. Specifically, some elements are taken into account as sadness, pessimism, suicidal thoughts/wishes, crying, agitation, loss of interest, indecisiveness, past failure, self-dislike, self-criticism, worthlessness, loss of energy, sleeping disturbances, irritability, changes in appetite, difficulties in attention, tiredness or chronic fatigue, and loss of interest in sex. It has Score range from 0 to 63: normal (0-13), mild depression (14-19), moderate depression (20-28) and severe depression (29-63) [31,32].
3. Disease activity was calculated by (DAS-28). It has four components which are tender joint count, swollen joint count, Erythrocyte Sedimentation Rate (ESR) and Visual Analogue Score (VAS).
4. Score which was as follows: score <2.6: remission, >2.6 and ≤ 3.2: low disease activity, >3.2 and ≤ 5.1: moderate disease activity, >5.1: High disease activity [33].
5. Rheumatoid Arthritis Disease Activity Index (RADAI-5) RADAI-5 is a five-item, self-administered RA-specific questionnaire that assesses global disease activity in the past 6 months and current disease activity in terms of joint swelling and tenderness, pain, duration of morning stiffness, and general health. The result can be easily calculated as follows: $(Q1+Q2+Q3+Q4+Q5)/5$. Scores between 0.0 and 1.4 indicate remission, 1.6 and 3.0 low disease activity, 3.2 and 5.4 moderate disease activity, and greater than 5.6 high disease activity [34,35].
6. The modified Health assessment questionnaire (MHAQ). It includes questions concerning perceived patient satisfaction regarding the same activities of daily living, along with perceived change in degree of difficulty.

The eight activities measured by the MHAQ are: Dressing and grooming, arising, eating, walking, hygiene, reach, grip, common

daily activities. Patients are asked to rate these daily activities on a scale ranging from 1 to 4 with: without difficulty, with some difficulty, with much difficulty, unable to do. The MHAQ may be calculated by adding all scored items and dividing by the total number of items answered to obtain the final score. It has score range from between 0.0-3.0: normal (MHAQ 0-0.4) mild (MHAQ 0.4-1.2), moderate (1.3-1.8) and severe (MHAQ >1.8) functional losses [36].

Rheumatoid Arthritis Quality of Life scale (RAQoL)

It consists of 30 statements describing the impact of RA and its treatment on the patient. Each statement has a simple yes/no response format. Scores range from 0 to 30 with a high score indicating poor QoL [37].

Visual Analogue Score (VAS)

The pain VAS is a continuous scale of 10 centimetres (100 mm) in length, anchored by 2 verbal descriptors, one for each symptom extreme. For pain intensity, the scale is most commonly anchored by "no pain" (score of 0) and "pain as bad as it could be" or "worst imaginable pain" (score of 100 [100 mm scale]). The score is determined by measuring the distance (mm) on the 10 cm line between the "no pain" anchor and the patient's mark using a ruler. A higher score indicates greater pain intensity. The cut off points on the pain VAS was: no pain (0-4 mm), mild pain (5-44 mm), moderate pain (45-74 mm), and severe pain (75-100 mm) [38].

Fatigue Severity Scale (FSS)

The scale contains nine items measuring the fatigue severity of the subjects during the past week. Each item is scored from 1 to 7. "1" indicates strong disagreement with the statement, while "7" indicates strong agreement. The total score is calculated by obtaining an arithmetic mean. A score of 4 or higher indicates severe fatigue [39]. Complete medical history and a full clinical examination were done to the patients. Laboratory tests was performed including C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR) 1st hour (according to modified Westergren method)

Data collection technique

The researcher interviewed the patients at the rheumatology in patient department face-to-face to ensure reliability and validity of data collection. First the questionnaires were pilot tested on 25 patients. The results of the pilot test were used for assessing the questionnaires regarding the simplicity and clarity. The Data from pilot study wasn't included in data analysis.

Statistical analysis

The data was processed in SPSS (Statistical Package for the Social Sciences) program. Within descriptive statistics continuous variables were characterized using classic (mean, the standard deviation). The differences between the values of continuous variables in two groups were examined using Student's t-test. The relation between continuous variables was measured with the Pearson correlation coefficient. The level of statistical significance

for all the tests carried out within the study was defined as $p < 0.05$.

Ethical considerations

There was an official approval from the general manager of Cairo University Hospitals. The study was explained to all participated patients and written Informed consent was obtained from them.

Results

In **Table 1**, the study included 200 patients with an average age of 26 years (18-56 years) and a mean age of onset of the disease of 26.5 years. The majority of the patients were females 69%. Most of the patients had school education and not working 73.5%, 65.5% respectively. Fifty nine percent were urban resident and the majority 80% was married. **Table 2** shows rheumatoid arthritis specific factors. The patients had moderate to severe depression; mean BDI score 21 ± 12.61 with moderate to severe disease activity where mean DAS-28 is 3.97 ± 1.19 . The patients showed to have moderate to severe functional loss and poor quality of life as mean MHAQ and RAQoL was 1.27 ± 0.63 and 17.845 ± 8.32 respectively. Regarding the severity of pain it was found that the patient experienced moderate pain and disease activity but with severe fatigue.

There were identified statistically significant correlations between BDI score with ESR ($r=0.537$) and CRP ($r= 0.654$). Correlation

Table 1 Demographic characteristic of the patients.

Demographic characteristics		No	%
Gender	Male	61	30.5
	Female	139	69.5
Education	School education	147	73.5
	Higher school or university	53	26.5
working status	Working	69	34.5
	Not working	131	65.5
Residence	Rural	82	41
	Urban	118	59
Marital status	Not married	40	20
	Married	160	80

Table 2 Rheumatoid arthritis specific factors.

Variables	Mean \pm Std. Deviation
Disease	6.75 \pm 4.32
Duration (Years)	
Ag of onset	26.5 \pm 7.27
Tender Joint counts	4.79 \pm 2.74
Swollen Joint counts	3.15 \pm 2.22
ESR	47 \pm 19.87
(Erythrocyte Sedimentation Rate)	
BDI	21 \pm 12.61
DAS 28	3.97 \pm 1.19
MHAQ	1.27 \pm 0.63
RAQoL	17.845 \pm 8.32
VAS-pain	48.44 \pm 7.89
RADAI-5	4.755 \pm 2.05
FSS	35.97 \pm 5.66

analysis showed a significant positive correlation between BDI score with both number of painful and swollen joints ($r=0.688, 0.59$) respectively ($p<0.01$). Statistically significant correlations were depicted between the score of BDI with the disease activity calculated by DAS-28 ($r=0.615$), the functional status assessed by MHAQ ($r=0.706$), Rheumatoid arthritis quality of life ($r=0.661$), Fatigue severity scale($r=0.734$) and RADAI-5 (0.647). The strongest correlation of ($r=0.829$) was with Visual analogue scale-pain (**Table 3**).

As shown in **Table 4** Mean BDI score was significantly higher among female patients compared to males ($p<0.01$). It was observed that patients who had high institute or university education their mean BDI score was significantly higher than those who had school education ($P=0.04$), also urban resident

patients scored higher than rural resident ($p=0.03$). Moreover not working patients was significantly higher in their mean score than working patients. Regarding marital status there was no significant difference in BDI score between married and unmarried patients.

As illustrated in **Figure 1**, nearly half of the patients 97 (48.5%) had moderate depression as scored by BDI, followed by 64 patients (32%) with mild depression. Then, 30 patients (15%) were normal. Nine patients (4.5%) were found to have severe depression.

Comparing the mean BDI in patients according to the disease activity calculated by DAS-28, it was shown that patients with severe disease activity had the highest mean value of BDI (38.1, $P<0.01$) (**Figure 2**).

Table 3 Correlation between BDI score and ESR, CPR, number of painful joints, number of swollen joints, disease activity, functional status, quality of life pain and fatigue.

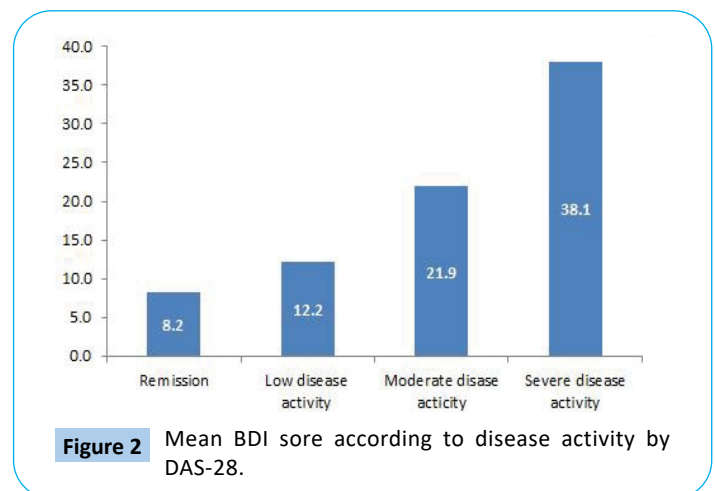
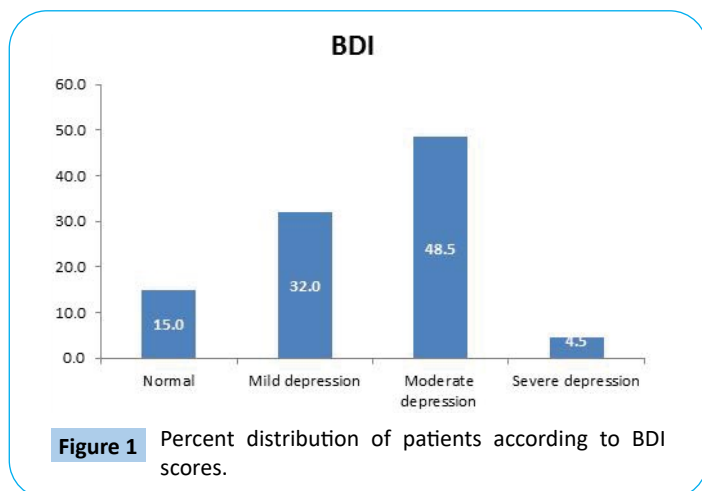
	ESR	CRP	No. of painful joints	No. of swollen joints	DAS-28 (score)	MHAQ (score)	RAQoL	VAS-pain	FSS	RADAI-5
BDI	0.537**	0.654**	0.688**	0.590**	0.615**	0.706**	0.661**	0.829**	0.734**	0.647**
	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01

**Significant at the level at 0.05

Table 4 Relation between demographic characteristics of patients and BDI score.

Demographic characteristics		Mean	SD	P value
Gender	Male	17.13	7.93	<0.01*
	Female	22.45	13.91	
Education	School education	19.28	12.31	0.04*
	High institute or university	25.13	12.56	
working status	Working	18.39	8.24	0.02*
	Not working	22.11	14.26	
Residence	Rural	17.62	10.36	0.003*
	Urban	23.06	13.57	
Marital status	Not married	19.25	9.56	0.377
	Married	21.23	13.27	

*Significant at the level at 0.05



As for MHAQ, the mean of BDI was highest among patients with severe functional loss [36], while in moderate functional loss it was 24.3. In patients with mild functional loss BDI was 17.1 and it was lowest 4.1 among patients with no functional loss ($p < 0.01$) (Figure 3).

Discussion

RA is a chronic systemic inflammatory disease which has a substantial impact on health. It leads to major functional disability compromising the physical and psychological aspects of quality of life [40-42]. Depression is a frequent disorder among RA [43,44] patients increasing the risk of mortality [19,42]. It is a silent comorbidity that usually neither recognized nor treated [45]. In 2002, a systematic review and meta-analysis done by Dickens et al. discovered that depression was frequently higher in patients with RA than in healthy individuals [46]. In 2013, another meta-analysis of 72 studies including 13,189 patients showed that the prevalence of major depression was 16.8% [47].

Depression is a common disorder among Egyptian RA patients [48]. It was shown that the prevalence of major depressive disorder in RA was high at least double that of the general population [49,50]. The present study discovered that approximately half of the patients were depressed where 48.5% had moderate depression and 4.5% had severe depression. Similarly it was shown that 45% of the patients had mostly moderate and severe depression, same as Sruamsiri et al. [51]. The results of the present study was more than that depicted by Mostafa and Radwan who found that the prevalence of depression among Egyptian RA patients was 15.29% [52] also Abdel-Nasser et al. reported a prevalence of 23% [88]. On the other hand studies showed higher prevalence 66% [53] and 80% [54]. These results are particularly alarming and it is required to monitor depressive disorder in RA patients [48].

Understanding factors associated with depression among RA patients is of high importance [55]. There has been discussion in literature about the factors influencing the development of depression among the patients. Disease activity was shown to be significantly related to depression [52]. In this study Patients with Severe disease activity measured by DAS-28 had the highest mean value of BDI. BDI score was shown to be significantly correlated

with DAS 28 and RADAI-5 score p value of < 0.01 . This correlation was previously found in the study of Pollard et al. [56] measuring the disease activity using DAS-28. Cadena et al. [57] Wolfe and Michaud, [58] Kotb [59] and Sheehy et al. [60] depicted strong associations between psychological status and disease activity similar to the current study results. Similarly, Walker et al. [61] and Raterman et al. [62] confirmed that depression among RA patient was associated with worsening disease activity. This finding was in agreement with Pincus et al. they reported that increasing disease activity predicts greater depression [63]. This can be explained that when the severity of the disease and inflammation increased the patient become unable to cope with social events so, they become more prone to depression [64].

On the other hand Cordingley et al. [65] depicted contradictory findings they found no statistically significant association between disease activity and depression levels by using Hospital Anxiety and Depression Scale. Also, Heimans et al. [66] depicted that severity of depression was associated with symptoms of arthritis like pain, but not disease activity.

There is no doubt that Physical disability and functional limitation are strong predictors and increasing the risk of depression among RA patients [67-73]. The participated patients in the current study were found to have moderate to severe functional loss measured by MHAQ questionnaire. The mean BDI was highest among patients with severe functional loss and BDI score was significantly positive correlated with MHAQ score. A multicentre prospective study included 641 RA patients suggested that HAQ-DI score was a predictor of patient depression [74] and that was similar to Masood et al. [75]. Similarly an American study of 172 patients showed that increased HAQ score was significantly associated with depression [50].

RA has a major, diverse effect on patients' quality of life [41]. It was depicted a significant correlated between BDI score and RAQoL in the current study. Similarly, Depression was shown to be significantly correlated with Quality of life [76,77].

It was found that the most important predictor of depression score was the VAS Pain [78]. Magni et al. found that pain increases depression and depression gives persistence and increase pain [79]; in the studies of Conner et al. along with those of Zautra et al. the patients with recurrent depression reported more levels of pain than those who without depression. This can be attributed to the fact that negative thoughts in depression affect the way in which patients perceive their somatic symptoms [80,81]. There was a strong positive correlation detected between BDI II and VAS pain in the present study. Similarly a strong correlation was demonstrated between the pain experienced by the patient (measured on the VAS) and the occurrence of depression symptoms ($BDI \geq 10$) [13]. This came in a line with Yilmaz and his colleagues who detected a positive correlation was between the BDI score with the VAS, DAS-28, and HAQ scores [82]. RA patients suffer from fatigue which is a dominant disturbing symptom [83-86]. As demonstrated in the present study there was as significant correlation between FSS score and BDI score, and that was found in previous studies [87,88].

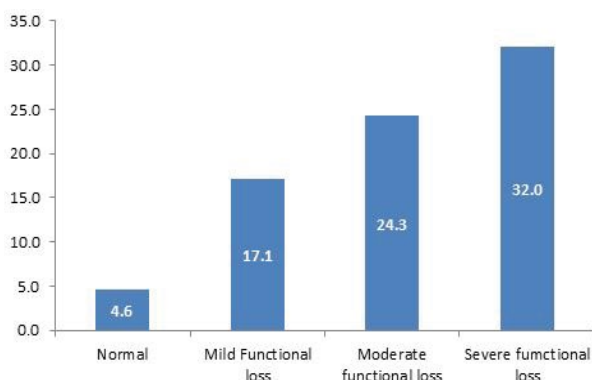


Figure 3 Mean BDI score according to functional loss by MHAQ.

The study showed that BDI score significantly correlates with the inflammatory parameters ESR and CPR. It was demonstrated that patients with major depression had increased levels of plasma C-reactive proteins [89,90]. That was similar to the findings depicted by Kotb et al. [59]. These findings were also similar to Alesci et al. study that reported elevated levels of CRP among depressed patients [91]. There are two hypotheses for the contribution of the systemic inflammation in RA to the high prevalence of depressive symptoms. First, RA disability prevents patients from functioning normally as they used to, so this generates feelings of loss and depression. Second, the pro-inflammatory cytokines which cause the acute flares in RA may have a direct neural impact in promoting sickness behaviour and corresponding depressive symptoms. Other study reported that this may be related to the shared pathophysiologic inflammatory pathway between depression and RA [60]. Contrary to the observations of the general population where ESR and CRP had no impact on depression symptoms in RA patients, that could be explained due to the fact that the patients were taking anti-inflammatory drugs [13].

Recently, the relationship between gender and depression in RA has become a focus in many studies [67,72,92]. It was revealed from the study that most of the RA patients were females 69.5% which was similar to a lot of studies as the disease mainly affects the females [93]. This may be related to the effect of estrogen hormone that predisposes to RA development, although androgen hormone has a protective role against the occurrence of RA [94]. The study showed that the mean BDI score was significantly higher in females compared to males. Lin and colleagues discovered in 2015 that women were at a particular risk of depression [92]. Also a retrospective study included more than 4000 patient showed that within the 5 years following RA diagnosis women were more likely to be diagnosed with depression when compared to men [95]. More recently, in a Taiwanese analysis included 3698 newly diagnosed adults

with RA it demonstrated that women, were having a higher risk more than men for developing depression. The relation between gender and depression in RA can be explained that men may adjust better to their disease than women. Another possibility is that male RA patients are less likely to disclose their depressive symptoms to their doctor than female patients.

In the present the mean BDI score was significantly higher in patients with high education and in those who were not working. Kwiatkowska et al. found that patient education was one of the factors that did not have an impact on the occurrence of depression symptoms in RA patients [67]; however they emphasized that professional activity is a factor which cause fewer depressive symptoms where professionally inactive patients have significantly more depressive symptoms than those who are professionally active. This highlights the importance of RA patients to keep working which is a factor that decreases the risk of depression, and that was confirmed in the literature [96,97]. Moreover, urban resident was significantly higher in depression scores than rural resident same as Abdel-Nasser et al. [98]. This was contradicted by Kwiatkowska et al. who found no difference in depressive symptoms regarding residence. The study found no significant difference between married and unmarried regarding BDI score.

Conclusion

In Conclusion depression among RA is a common disorder related to disease severity and quality of life, yet it still unrecognized. It was found that the patients haven't been screened for depression before and didn't discuss their symptoms with their physicians. It recommended incorporating assessment and periodic screening of comorbid depression in the management protocols of RA patients. This can help early diagnosis, treatment and avoiding full blown picture of depression with its negative impact on the course of RA disease.

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