



Research Paper

The impact of anxiety and depression on rheumatoid arthritis patients: A study in a tertiary hospital

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ABSTRACT

Depression and anxiety are prevalent psychiatric comorbidities of rheumatoid arthritis (RA), affecting disease prognosis and patients' quality of life. However, there is insufficient literature regarding this topic in Saudi Arabia. Thus, we sought to identify the risk of depression and anxiety, and the associated socio-demographic, clinical, and medical risk factors among rheumatoid arthritis patients at XXX, YYY. In a non-interventional cross-sectional study, the prevalence and correlations of anxiety and depression in 92 patients with RA at XXX University in YYY were investigated. Laboratory data were collected from the patient hospital records. Sociodemographic data and comorbid conditions were self-reported using an online questionnaire. RA disease activity was assessed using the Health Assessment Questionnaire (HAQ). Depression was assessed using the 9-item Patient Health Questionnaire (PHQ9). Anxiety was assessed using the 7-item General Anxiety Disorder Scale (GAD7). Based on GAD7 and PHQ9 scores, 63% of the participants were identified as being at risk of anxiety and depression. Findings regarding the severity of depression and anxiety were positively linked to the level of pain, severity of RA, and quality of life. Levels of depression were significantly associated with low levels of vitamin B12 and the use of steroids. There was a significant association of anxiety with age and steroid use. A large percentage of RA patients suffer from depression and anxiety symptoms. Therefore, it is important to screen for psychological difficulties among RA patients and to offer them social support, as this could improve their prognosis.

Yasser Bawazir^{1*}, Marwa Abdelmoaty², Nouf Aljahdaly², Khaled Alghamdi², Abdulrahman Alghamdi², Mohammad Mustafa³, Sulhi Alfakeh¹

¹Department of Internal Medicine, King Abdulaziz University, Jeddah 21589, Saudi Arabia

²Faculty of Medicine, King Abdulaziz University, Jeddah 21589, Saudi Arabia

³Internal Medicine, University of Jeddah, Jeddah 23456, Saudi Arabia

*Corresponding author. E-mail: ymbawazir@kau.edu.sa

Key words: Anxiety, depression, Health Assessment Questionnaire, rheumatoid arthritis, Saudi Arabia.

ABBREVIATIONS

ANOVA; analysis of variance, **DMARDs;** disease-modifying antirheumatic drugs, **DSM;** Diagnostic and Statistical Manual for Mental Disorders, **GAD7;** 7-item General Anxiety Disorder Scale, **HAQ;** Health Assessment Questionnaire, **NRS;** numeric pain rating scale,

PHQ9; 9-item Patient Health Questionnaire, **RA;** rheumatoid arthritis, **UK;** United Kingdom, **USA;** United States of America.

INTRODUCTION

Psychiatric disorders, including depression and anxiety, are common comorbidities of rheumatoid arthritis (RA) that

might affect the patient's perception of pain, functional disability, and quality of life (Abdel et al., 2016; Nas et al.,

2011; Psychiatry.org, 2020). RA is an autoimmune disease of unknown etiology that commonly affects joints, causing

The prevalence of RA globally ranges from 0.3% to 1% and is more prevalent among women and in developed countries (<https://www.who.int/chp/topics/rheumatic/en/>). The 2010 Global Burden of Disease study reported an estimated RA prevalence of 0.24% (Cross et al., 2010). In Saudi Arabia, 2 studies showed an estimated prevalence among the general adult population of 0.22% (Al-Dalaan et al., 1998) and 0.3% (Albishri et al., 2015). Anxiety and mood disorders, such as depression, have been associated with RA. The nature of the disease contributes to psychological struggles (El-Miedany and El-Rasheed, 2002; VanDyke et al., 2004) and increases the patients' anxiety about their well-being. Furthermore, it adversely affects patients' social life and personal relationships. With disease progression, patients tend to become more dependent on others, which might make them feel helpless. All of these factors again fuel depression and anxiety in these patients (Covic et al., 2012).

Depression is a common and serious mental illness that affects how individuals feel, think, and act. It can lead to a variety of emotional and physical problems and functional disabilities (Psychiatry.org, 2020). People with anxiety disorders usually have recurrent intrusive thoughts or concerns. They may avoid certain situations out of worry. Furthermore, they may have physical symptoms, such as sweating, trembling, dizziness, or a rapid heartbeat (<https://www.apa.org/topics/anxiety/index>, 2019). Generally, the incidence and prevalence of depression and anxiety are markedly higher in the RA population than in a matched non-RA population (Marrie et al., 2018). Many studies have demonstrated the association of RA with depression and anxiety (El-Miedany and El-Rasheed, 2002; VanDyke et al., 2004; Covic et al., 2012; Matcham et al., 2013; Murphy et al., 2012) and approximately 16–44% of RA patients have met the Diagnostic and Statistical Manual for Mental Disorders (DSM) criteria for depression, and approximately 27–70% have met the DSM criteria for anxiety. Additionally, some studies (Kojima et al., 2009; Lee et al., 2009; Ozcetin et al., 2007) have suggested that depression and anxiety worsen the prognosis of RA in terms of pain and functional disability. Several factors are associated with an increased risk of mental illness comorbid with RA: marital status, where unmarried patients are more prone to developing mental illness (Abdel-Nasser et al., 1998; Fitzpatrick et al., 1991), young age (Wright et al., 1998), and lower education level (Leigh et al., 1992; Vlieland et al., 1994).

In contrast, a meta-analysis of 12 studies showed that demographic factors do not increase the risk of developing mental illness, although the level of pain does increase this risk (Dickens et al., 2003). Moreover, in RA patients with

inflammation and damage to the joint tissue, leading to long-standing or chronic pain and deformity (CDC, 2020).

comorbid mental illness, smoking (Alouffi et al., 2018) and medication adherence (Vallerand et al., 2019) can alter the prognosis of the disease. Proper and efficient antidepressant medication (Baune and Eyre 2010), psychotherapy (Keefe and Somers, 2010) and social support help to improve pain, functional status, and quality of life in the RA population (Matcham et al., 2013; Danoff-Burg and Revenson, 2005). To our knowledge, only one previous study on this topic has been conducted in Saudi Arabia and revealed a prevalence of depression of 18% among RA patients at King Abdulaziz University Hospital in Jeddah between 2008 and 2010 (Attar, 2014). However, no research has been conducted in Saudi Arabia regarding anxiety and the impact of both anxiety and depression on RA disease activity. Thus, this study aimed to determine the prevalence of anxiety and depression among RA patients at XXX Hospital and to establish their correlation with socio-demographic factors.

METHODS

Study design, setting, and participants

A descriptive cross-sectional study was conducted at XXX University Hospital (AAA), from January 1, 2020, to April 1, 2020, and included RA patients being followed-up in AAA. All patients between 18 and 70 years of age who were diagnosed with RA according to the 2010 American College of Rheumatology/European League against Rheumatism criteria were eligible to participate in the study. Patients older than 70 years or younger than 18 years of age were excluded from the study. Thus, of 189 patients, 11 were excluded because of age criteria. We attempted to contact the remaining 178 patients through telephone calls and WhatsApp. Of these, 92 patients agreed to participate, 18 patients refused to participate, and 68 patients did not have a valid contact method.

Data collection

The data were recorded in 2 parts. First, from hospital records, we obtained the patient's laboratory results, socio-demographic data (including age, gender, nationality, smoking status, height, and weight), telephone number, and comorbid conditions (including hypertension, diabetes, stroke, ischemic heart diseases, chronic obstructive pulmonary diseases, and gastroesophageal reflux disease). Second, using a secure online link, patients completed three questionnaires by self-reporting: the Health Assessment Questionnaire (HAQ), to assess RA disease activity; the 9-

item Patient Health Questionnaire (PHQ9), to assess depression; and the 7-item General Anxiety Disorder Scale (GAD7), to assess anxiety.

the HAQ. It has been translated and validated in Arabic and has shown high internal consistency (Cronbach's alpha = 0.979). Reliability analysis was performed on the Arabic HAQ scale, which comprises 20 items. Cronbach's alpha showed the questionnaire to reach acceptable reliability ($\alpha = 0.949$). The HAQ consists of 8 subscales and includes assigned aides and devices specific to each subscale: 1) dressing and grooming, 2) arising, 3) eating, 4) walking, 5) hygiene, 6) reach, 7) grip, and 8) common daily activities. Patients reported the amount of difficulty they experienced in performing activities during the last week. Each question has 4 possible answers: without any difficulty (score 0), with some difficulty (score 1), with much difficulty (score 2), and unable to do (score 3) (El-Meidany et al., 2003). Rheumatoid arthritis pain and the impact of RA on patients' lives were assessed using a numeric pain rating scale (NRS, min = 0, max = 10).

PHQ9 questionnaire

The Arabic 9-item PHQ9 was used to diagnose the presence and severity of depression over the last 2 weeks, which included the level of interest in doing things, feeling down or depressed, difficulty with sleeping, energy levels, eating habits, self-perception, ability to concentrate, speed of functioning, and thoughts of suicide. Each of the 9 items were scored from "0" (not at all) to "3" (nearly every day). The total score ranges from 0 to 27, with 0–4 representing no depression, 5–9 mild depression, 10–14 moderate depression, 15–19 moderately severe depression, and 20–27 severe symptoms of depression. The Arabic version showed internal consistency with Cronbach's alpha of 0.857 (AlHadi et al., 2017). Reliability analysis was carried out on the Arabic PHQ9 scale, which revealed that it had acceptable reliability (Cronbach's alpha = 0.915).

GAD-7 questionnaire

Anxiety was assessed using the Arabic GAD-7. In this questionnaire, 7 items questioned the patient about anxiety symptoms during the last 2 weeks. Response options were "not at all," "several days," "more than half the days," and "nearly every day." Scores range from 0 to 21, with scores of 6–10, 11–15, and >15 representing mild, moderate, and severe anxiety, respectively, whereas scores 0–5 are considered negative. In terms of internal consistency, Cronbach's alpha for the Arabic version was 0.763 (AlHadi et al., 2017). Reliability analysis of the Arabic GAD-7 scale

RA disease activity

RA disease activity was assessed using the Arabic version of

yielded a Cronbach's alpha of 0.924, which showed that the questionnaire had acceptable reliability.

Data analysis

The data were analyzed using IBM SPSS version 23 (IBM Corp., Armonk, NY, USA) and were visually presented using GraphPad Prism version 8 (GraphPad Software, Inc., San Diego, CA, USA). Simple descriptive statistics were used to define the characteristics of the study variables in the form of counts and percentages for the categorical and nominal variables, and means and standard deviations for continuous variables. To establish a relationship between categorical variables, this study used the chi-square test. When comparing more than 2 groups, a one-way analysis of variance with least significant difference (LSD) test as a post hoc test was used. These tests were performed with the assumption of a normal distribution. The Games-Howell test for multiple groups was used as an alternative for the LSD test. Finally, a conventional p-value <0.05, was used to reject the null hypothesis.

Ethical review

The study was approved by the Unit of Biomedical Ethics at King Abdulaziz University (Baune and Eyre 2010; Fitzpatrick et al., 1991). All participants provided written informed consent to participate in the study and were assured of their confidentiality.

RESULTS

Participants had a mean age of 47.63 ± 10.9 (min = 24, max = 67) and the majority were female (93.5%, n = 86), Saudi nationals (68.5%, n = 63), non-smokers (97.8%, n = 90), married (68.5%, n = 63), with High School-or College-level education (51.1%, n = 47), and earning less than 10,000 Saudi Riyals monthly (66.3%, n = 61), as shown in **Table 1**. Regarding medical history, most subjects had an RA duration of more than 10 years (52.2%, n = 48). Almost two-thirds had seropositive disease (62.6%, n = 57), and there anti-CCP levels were 60.2% (n = 50). The majority of subjects were on disease-modifying anti-rheumatic drugs (DMARDs; 94.6%, n = 87) (**Table 2**). Of the patients, 10.9% (n = 10) were diagnosed with a lifetime of mental or psychiatric illness. More than half of patients had normal levels of vitamin B12 (74.2%, n = 49), thyroid-stimulating hormone (80.0%, n = 60), and folate/folic acid (60.9%, n =

14). In contrast, approximately three-fourths of them (76.4%, n = 68) had low levels of vitamin D (Table 2). The depression level of patients was assessed using the PHQ9, as shown in Table 3. Overall, the majority of the patients (63.0%, n = 58) had a risk of developing depression, of which 8.7% (n=8) had severe; 9.8% (n=9) had moderately

severe; 16% (n=17.4), 17.4% had moderate (n=16), and 27.2% had mild (n=25) depression. Only 37% (n=34) of the patients had no sign of depression according to the PHQ assessment, having a mean PHQ9 score of 8.37 ± 6.6 . The mean HAQ7 final score was 1.28 ± 0.8 , the mean RA pain severity score was 5.26 ± 2.8 , and the mean score for the

Table 1: Patients' demographic data.

Demographics	N	Min	Max	Mean	SD
Age (years)	92	24	67	47.63	10.9
BMI (kg/m ²)	92	19	68	30.54	8.2
		Count		%	
Total		92		100.0	
Gender	Male	6		6.5	
	Female	86		93.5	
Nationality	Saudi	63		68.5	
	Non-Saudi	29		31.5	
Smoking status	Yes	2		2.2	
	No	90		97.8	
BMI Categories	Healthy	25		27.2	
	Overweight	24		26.1	
	Obese	43		46.7	
Marital status	Married	63		68.5	
	Single	11		12.0	
	Divorced	6		6.5	
	Widowed	12		13.0	
Educational level	Non	13		14.1	
	Primary	20		21.7	
	Elementary	12		13.0	
	High school	17		18.5	
	Collage	30		32.6	
Financial status	> 10K	61		66.3	
	10–15K	17		18.5	
	< 15K	14		15.2	

BMI, body mass index.

impact of RA on life was 5.73 ± 3.1 in the participants (Table 4). An almost equal distribution of the subjects were found to have mild to moderate disability (41.3%, n = 38) and moderate to severe disability (40.2%, n = 37), according to the HAQ. In addition, the majority of them had a mild NRS pain score for RA (54.3%, n = 50). Most responded favorably to an offer for visiting a psychiatric clinic (56.5%, n = 52). Anxiety and depression was present in almost two-thirds (63%, n = 58) of the patients and absent in about one-third (37.0%, n = 34) of the studied patients based on GAD7 and PHQ9 measurement scales and, respectively. The association of patient GAD7 scores with RA severity is shown in Table 5.

Prevalence of depression and anxiety risk in RA patients

According to the one-way ANOVA test at the 0.005 level, there were significant differences in GAD7 scores according to the HAQ score ($p < 0.001$). More specifically, a significantly lower mean HAQ score was observed for participants without anxiety (0.88 ± 0.8) than for those with moderate and severe anxiety according to GAD7 scores. There were also significant differences in GAD7 scores in terms of the mean RA pain severity scores ($p < 0.001$) and impact on life scores ($p < 0.001$). More specifically, significantly higher mean RA pain severity (7.29 ± 2.0) and impact on life scores (8.18 ± 1.6) were observed for subjects with severe anxiety than for those

without or with mild anxiety. Chi-square analysis also revealed significant differences between GAD7 scores relative to the HAQ scores ($p = 0.001$). More specifically, a significantly higher proportion of patients who were classified as moderately to severely disabled on the HAQ scale were found to have mild to severe symptoms of anxiety on the GAD7 scores (81.1%). Of those without anxiety according to their GAD7 scores, 60.5% ($n = 23$) had

mild to moderate disability on the HAQ assessment. The same test showed that there were also significant differences in the GAD7 scores of subjects in terms of the RA pain NRS scores ($p = 0.007$). More specifically, there were significantly more patients with mild pain, according to the NRS scores, who had no anxiety (54.0%, $n = 27$), than there were with anxiety, according to the GAD7. Lastly, there were significant differences in the GAD7 scores of

Table 2: Medical history of the studied patients.

Medical History		Count	%
Total		92	100.0
Duration of RA since diagnosis	< 5 years	21	22.8
	5–10 years	22	23.9
	> 10 years	48	52.2
	Not known	1	1.1
Diagnosis of lifetime mental or psychiatric illness		10	10.9
Prescription of medication for lifetime mental or psychological illness		8	8.7
Diabetes mellitus		14	15.2
Hypertension		13	14.1
Stroke		2	2.2
Ischemic heart disease		3	3.3
Gastroesophageal reflux disease		5	5.4
Chronic obstructive pulmonary disease		1	1.1
RF		34	37.4
Anti-CCP		50	60.2
Current medications Steroids		13	14.1
Current medications DMARDS		87	94.6
Current medications biological		34	37.0
Seropositivity	Seropositive	57	62.6
	Seronegative	34	37.4
	Missing	1	
Vit-B12	Normal	49	74.2
	Low	17	25.8
	Missing	26	
Vit-D	Normal	21	23.6
	Low	68	76.4
	Missing	3	
TSH	Normal	60	80.0
	Low	4	5.3
	High	11	14.7
	Missing	17	
Folic Acid	Normal	14	60.9
	Low	1	4.3
	High	8	34.8
	Missing	69	

RA, rheumatoid arthritis; DMARDS, Disease-modifying antirheumatic drugs; TSH, thyroid-stimulating hormone; CCP, cyclic citrullinated peptide; RF, rheumatoid factor; vit, vitamin.

participants in terms of their response to the offer of a visit to a psychiatric clinic ($p = 0.004$). More specifically, a large number of patients responded favorably to this offer (56.5%, $n=52$). Most of these patients (78.8%, $n=41$) were suffering from anxiety. On the other hand, of the patients who declined the offer (43.5%, $n = 40$), a significant number also suffered from symptoms of anxiety (42.5%, $n=17$). More specifically, a significantly higher proportion of patients who responded favorably to this offer had GAD7 scores below 6 (57.5%, $n = 23$) than had GAD7 scores ≥ 6 .

Impact of depression on RA severity

The association of depression levels of patients (based on the PHQ relative to RA scores) was also evaluated (Table 6). There were significant differences in the PHQ-based depression levels of participants relative to the mean HAQ final score ($p < 0.001$) according to the one-way ANOVA test. More specifically, a significantly higher mean HAQ final score was found in patients with severe depression (2.06 ± 0.04) than in those without or with moderate depression,

Table 3: Measurement of depression level of rheumatoid arthritis patients by means of the 9-item Patient Health Questionnaire (PHQ9)

Patient Health Questionnaire:		Count	%
Total		92	100.0
PHQ1: Little interest or pleasure in doing things	Not at all	35	38.0
	Several days	35	38.0
	Over half the days	12	13.0
	Nearly every day	10	10.9
PHQ2: Feeling down, depressed, or hopeless	Not at all	29	31.5
	Several days	37	40.2
	Over half the days	18	19.6
	Nearly every day	8	8.7
PHQ3: Trouble falling or staying asleep, or sleeping too much	Not at all	23	25.0
	Several days	29	31.5
	Over half the days	22	23.9
	Nearly every day	18	19.6
PHQ4: Feeling tired or having little energy	Not at all	16	17.4
	Several days	32	34.8
	Over half the days	25	27.2
	Nearly every day	19	20.7
PHQ5: Poor appetite or overeating	Not at all	27	29.3
	Several days	40	43.5
	Over half the days	18	19.6
	Nearly every day	7	7.6
PHQ6: Feeling bad about yourself, or that you are a failure, or have let yourself or your family down	Not at all	47	51.1
	Several days	24	26.1
	Over half the days	10	10.9
	Nearly every day	11	12.0
PHQ7: Trouble concentrating on things, such as reading the newspaper or watching television	Not at all	51	55.4
	Several days	20	21.7
	Over half the days	10	10.9
	Nearly every day	11	12.0
PHQ8: Moving or speaking so slowly that other people could have noticed? Or so fidgety or restless that you have been moving a lot more than usual	Not at all	65	70.7
	Several days	12	13.0
	Over half the days	8	8.7
	Nearly every day	7	7.6
PHQ9: Thoughts that you would be better off dead, or thoughts of hurting yourself in some way	Not at all	76	82.6
	Several days	12	13.0
	Over half the days	2	2.2
	Nearly every day	2	2.2
Patient Health Questionnaire	Normal	34	37.0

	Mild	25	27.2		
	Moderate	16	17.4		
	Moderately severe	9	9.8		
	Severe	8	8.7		
PHQ9 score	N	Min	Max	Mean	SD
	92	0	27	8.37	6.6

while the mean HAQ final score was significantly lower for subjects without (0.96 ± 0.7) than for subjects with moderate to severe depression. One-way ANOVA also

revealed significant differences in the depression levels of patients with respect to the RA pain severity score factor ($p < 0.001$). More specifically, a significantly lower mean RA

Table 4: Pain scores, impact on life and responses to an offer to visit a psychiatry clinic.

Variables	N	Min	Max	Mean	SD
Health assessment questionnaire final scores	92	0	3	1.28	0.8
RA pain severity score	92	0	10	5.26	2.8
RA impact on life score	92	0	10	5.73	3.1
				Count	%
Total				92	100.0
Health assessment questionnaire	(0–1) Mild to moderate disability			38	41.3
	(1–2) Moderate to severe disability			37	40.2
	(2–3) Severe to very severe disability			17	18.5
Numeric pain rating scale for RA pain scores	Mild			50	54.3
	Moderate			19	20.7
	Severe			23	25.0
Response to an offer to visit a psychiatric clinic	Yes			52	56.5
	No			40	43.5

Table 5: Association of patients general anxiety levels with respect to rheumatoid arthritis severity scores.

Variables	Total	General Anxiety Disorder				p-value	
		Normal	Mild	Moderate	Severe		
Health assessment questionnaire final score ^c	92	0.88 ± 0.8^A	1.26 ± 0.6^{AB}	1.63 ± 0.7^B	1.69 ± 0.7^B	<0.001 ^a	
RA pain severity score ^c	92	3.82 ± 2.8^A	5.10 ± 2.4^{AB}	6.10 ± 2.5^{BC}	7.29 ± 2.0^C	<0.001 ^a	
RA impact on life score ^d	92	3.65 ± 2.6^A	5.40 ± 2.6^{AB}	7.43 ± 2.8^{BC}	8.18 ± 1.6^C	<0.001 ^a	
Total	92	34 (37.0%)	20(21.7%)	21(22.8%)	17(18.5%)	-	
Health Assessment Questionnaire	(0–1) Mild to moderate disability	38	23(60.5%)	7(18.4%)	5(13.2%)	3(7.9%)	0.001 ^b
	(1–2) Moderate to severe disability	37	7(18.9%)	12(32.4%)	10(27.0%)	8(21.6%)	
	(2–3) Severe to very severe disability	17	4(23.5%)	1(5.9%)	6(35.3%)	6(35.3%)	
Numeric pain rating scale for RA pain scores	Mild	50	27(54.0%)	10(20.0%)	9(18.0%)	4(8.0%)	0.007 ^b
	Moderate	19	3(15.8%)	6(31.6%)	5(26.3%)	5(26.3%)	
	Severe	23	4(17.4%)	4(17.4%)	7(30.4%)	8(34.8%)	
RA patients' response to an offer to visit a psychiatric clinic	Yes	52	11(21.2%)	14(26.9%)	14(26.9%)	13(25.0%)	0.004 ^b
	No	40	23(57.5%)	6(15.0%)	7(17.5%)	4(10.0%)	

a, significant at the 5% level based on one-way analysis of variance

b, significant at the 5% level based on the chi-squared test
c, Post hoc test= least significant difference.
d, Post hoc test = Games-Howell
RA, rheumatoid arthritis

pain severity score was observed for participants without depression (4.12 ± 2.9) than for those with mild to severe depression. Significant differences were also found in the depression levels of subjects relative to the score for the impact of RA on their lives ($p < 0.001$). More specifically, a significantly lower mean impact on life score was observed for patients without (3.65 ± 2.6) than for patients with mild to severe depression. Similar significant differences in depression levels were found in participants with respect to the HAQ scale results ($p = 0.010$). More specifically, a significantly higher proportion of patients classified as having mild to moderate (52.6%, $n = 20$), and moderate to severe disability (32.4%, $n = 12$) according to the HAQ assessment, had normal depression levels compared with other depression levels. Moreover, significant differences were also found in the depression levels of patients relative

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Table 6: Association of depression levels of patients (based on the Patient Health Questionnaire) relative to rheumatoid arthritis pain and impact on life scores.

Variables	Total	Patient Health Questionnaire					p-value	
		Normal	Mild	Moderate	Moderately Severe	Severe		
Health assessment questionnaire final score ^c	92	0.96 ± 0.7 ^A	1.21 ± 0.7 ^{AB}	1.45 ± 0.6 ^{BC}	1.75 ± 0.8 ^{CD}	2.06 ± 0.4 ^D	<0.001 ^a	
RA pain severity score ^c	92	4.12 ± 2.9 ^A	4.64 ± 2.6 ^{AB}	6.88 ± 2.1 ^C	6.33 ± 2.4 ^{BC}	7.63 ± 1.7 ^C	<0.001 ^a	
RA impact on life score ^c	92	3.65 ± 2.6 ^A	5.16 ± 2.5 ^B	7.94 ± 1.9 ^C	8.67 ± 1.9 ^C	8.63 ± 1.5 ^C	<0.001 ^a	
Total	92	34 (37.0%)	25 (27.2%)	16 (17.4%)	9 (9.8%)	8 (8.7%)	-	
Health assessment questionnaire	(0–1) Mild to moderate disability	38	20(52.6%)	12 (31.6%)	4 (10.5%)	2 (5.3%)	0 (0.0%)	0.010 ^a
	(1–2) Moderate to severe disability	37	12 (32.4%)	9 (24.3%)	9 (24.3%)	3 (8.1%)	4 (10.8%)	
	(2–3) Severe to very severe disability	17	2 (11.8%)	4 (23.5%)	3 (17.6%)	4 (23.5%)	4 (23.5%)	
Numeric Pain Rating scale for RA pain scores	Mild	50	25 (50.0%)	16 (32.0%)	5 (10.0%)	3 (6.0%)	1 (2.0%)	0.013 ^a
	Moderate	19	3 (15.8%)	5 (26.3%)	4 (21.1%)	4 (21.1%)	3 (15.8%)	
	Severe	23	6 (26.1%)	4 (17.4%)	7 (30.4%)	2 (8.7%)	4 (17.4%)	
RA patients' response to an offer to visit a psychiatric clinic	Yes	52	12 (23.1%)	17 (32.7%)	10 (19.2%)	7(13.5%)	6 (11.5%)	0.032 ^a
	No	40	22 (55.0%)	8 (20.0%)	6 (15.0%)	2 (5.0%)	2 (5.0%)	

a. significant at the 5% level based on one-way analysis of variance

b. significant at the 5% level based on the chi-squared test

c. Post hoc test= least significant difference.

RA, rheumatoid arthritis

to the NRS RA pain scores ($p = 0.013$). More specifically, a significantly higher rate of participants with mild (50.0%, $n = 25$) and severe (26.1%, $n = 6$) RA pain had normal levels of depression in comparison with other degrees of depression. Lastly, significant differences were observed in the depression levels of participants in terms of their response to the offer of a visit to a psychiatric clinic ($p = 0.032$). More specifically, a significantly higher proportion of patients who favored the offered visit had depression (76.9%, $n=40$), while a significantly higher proportion of

patients who declined the offer had no depression (55.0%, $n = 22$).

Association of demographic, clinical, and socioeconomic factors and comorbidities with anxiety among RA patients

The association of anxiety level of patients with respect to demographic, clinical, socioeconomic factors, and comorbidities was then assessed. Significant differences in the anxiety levels of subjects were only found relative to age ($p = 0.011$) according to one-way ANOVA (Table 7). More

specifically, a significantly higher mean GAD7 score was observed for participants without anxiety (52.41 ± 9.7) than for those with mild and moderate anxiety. No other demographic factors showed any significant differences based on the one-way ANOVA ($p > 0.05$). Supplementary Table 3 shows the association between anxiety and the comorbidities of patients. There were no significant differences in the anxiety levels of subjects in terms of factors such as disease duration, diagnoses, or comorbidities ($p > 0.05$). A similar test was performed to analyze the association of

participants' anxiety levels relative to their respective clinical results (Table 8). The chi-square test revealed significant differences ($p = 0.035$) in the anxiety levels of patients in terms of current use of steroid medications. More specifically, a significantly high proportion of patients who were

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Table 7: To identify the significance and association of demographic, clinical, socioeconomic factors and comorbidities with depression and anxiety among rheumatoid arthritis patients.

Demographics		Total	General Anxiety Disorder				p-value
			Normal	Mild	Moderate	Severe	
Age (years) ^b		92	52.41 ± 9.7 ^A	44.75 ± 9.9 ^B	43.71 ± 11.6 ^B	46.29 ± 11.1 ^{AB}	0.011 ^a
BMI (kg/m ²)		92	32.18 ± 9.2	29.07 ± 8.3	29.73 ± 7.3	29.96 ± 7.3	0.524
Total		92	34 (37.0%)	20 (21.7%)	21 (22.8%)	17 (18.5%) ^A	-
Gender	Male	6	5 (83.3%)	0 (0.0%)	0 (0.0%)	1 (16.7%)	0.086
	Female	86	29 (33.7%)	20 (23.3%)	21 (24.4%)	16 (18.6%)	
Nationality	Saudi	63	23 (36.5%)	17 (27.0%)	13 (20.6%)	10 (15.9%)	0.296
	Non-Saudi	29	11 (37.9%)	3 (10.3%)	8 (27.6%)	7 (24.1%)	
Smoking status	Yes	2	1 (50.0%)	0 (0.0%)	1 (50.0%)	0 (0.0%)	0.664
	No	90	33 (36.7%)	20 (22.2%)	20 (22.2%)	17 (18.9%)	
BMI Categories	Healthy	25	5 (20.0%)	9 (36.0%)	7 (28.0%)	4 (16.0%)	0.130
	Overweight	24	8 (33.3%)	3 (12.5%)	6 (25.0%)	7 (29.2%)	
	Obese	43	21 (48.8%)	8 (18.6%)	8 (18.6%)	6 (14.0%)	
Marital status	Married	63	24 (38.1%)	15 (23.8%)	13 (20.6%)	11 (17.5%)	0.202
	Single	11	4 (36.4%)	2 (18.2%)	4 (36.4%)	1 (9.1%)	
	Divorced	6	0 (0.0%)	0 (0.0%)	3 (50.0%)	3 (50.0%)	
	Widowed	12	6 (50.0%)	3 (25.0%)	1 (8.3%)	2 (16.7%)	
Educational level	Non	13	7 (53.8%)	0 (0.0%)	3 (23.1%)	3 (23.1%)	0.590
	Primary	20	7 (35.0%)	6 (30.0%)	6 (30.0%)	1 (5.0%)	
	Elementary	12	4 (33.3%)	2 (16.7%)	4 (33.3%)	2 (16.7%)	
	High school	17	7 (41.2%)	4 (23.5%)	2 (11.8%)	4 (23.5%)	
	Collage	30	9 (30.0%)	8 (26.7%)	6 (20.0%)	7 (23.3%)	
Financial Status	<10K	61	21 (34.4%)	11 (18.0%)	16 (26.2%)	13 (21.3%)	0.707
	10–15 K	17	8 (47.1%)	5 (29.4%)	2 (11.8%)	2 (11.8%)	
	> 15 K	14	5 (35.7%)	4 (28.6%)	3 (21.4%)	2 (14.3%)	

^asignificant at the 5% level based on one-way analysis of variance

^b.Post hoc= least significant difference.

BMI, body mass index;

medicated with steroids (14%, n=13) had anxiety (77%, n=10), while a significantly high number of subjects who were not medicated with steroids (86%,n=79) also had anxiety (60.7%, n = 48). On the other hand, a notable number of patients who were classified as seropositive (38.6%, n = 22), as well as of those who were classified as seronegative (35.3%, n = 12), had no anxiety. However, these were not significantly different from the numbers of patients with any level of anxiety (p > 0.05).

Association of demographic, clinical, and socioeconomic factors and comorbidities with depression among RA patients

The association of PHQ-based depression results of patients with respect to demographic, clinical, and socioeconomic factors, and comorbidities was also determined. There were no significant differences in the depression levels of

participants with respect to any of the studied demographic and socio-economic factors, or comorbidities (p > 0.05), according to chi-squared tests (Supplementary Tables 4 and 5). However, there were significant differences in depression levels of subjects with respect to the level of vitamin B12 (p = 0.039), as shown in Table 9. More specifically, a significantly higher proportion of patients with low levels of vitamin B12 had depression (70.6%,n=12) than no depression (29.4%,n=5). In addition, a notably large number of patients with normal levels of vitamin B12 had depression (57.2%, n=28). Chi-squared analysis also revealed significant differences in the depression levels of subjects relative to the current steroid medication factor (p = 0.034). More specifically, a significantly higher number of patients who were taking steroids as medication (14%, n=18) had depression (77%, n = 10). A large number of patients who were not taking steroids as medication (86%, n=79) also had depression (60.8%,n=48). More patients who were classified as

seropositive (35.1%, n = 20) or as seronegative (41.2%, n = 14) were without depression, but these rates were not

statistically significantly different from those who had any level of depression ($p > 0.05$).

Table 8: Association of anxiety levels of participants relative to their respective clinical results

Variables	Total	General Anxiety Disorder				p-value	
		Normal	Mild	Moderate	Severe		
Total	92	34 (37.0%)	20 (21.7%)	21 (22.8%)	17 (18.5%)	-	
RF	Positive	34	13 (38.2%)	5 (14.7%)	11 (32.4%)	5 (14.7%)	0.323
	Negative	57	21 (36.8%)	14 (24.6%)	10 (17.5%)	12 (21.1%)	
Anti-CCP	Positive	50	19 (38.0%)	10 (20.0%)	11 (22.0%)	10 (20.0%)	0.989
	Negative	33	13 (39.4%)	6 (18.2%)	8 (24.2%)	6 (18.2%)	
Seropositivity	Seropositive	57	22 (38.6%)	11 (19.3%)	14 (24.6%)	10 (17.5%)	0.920
	Seronegative	34	12 (35.3%)	8 (23.5%)	7 (20.6%)	7 (20.6%)	
Vit-B12	Normal	49	21 (42.9%)	9 (18.4%)	12 (24.5%)	7 (14.3%)	0.458
	Low	17	5 (29.4%)	4 (23.5%)	3 (17.6%)	5 (29.4%)	
Vit-D	Normal	21	6 (28.6%)	6 (28.6%)	4 (19.0%)	5 (23.8%)	0.531
	Low	68	28 (41.2%)	13 (19.1%)	15 (22.1%)	12 (17.6%)	
TSH	Normal	60	21 (35.0%)	13 (21.7%)	12 (20.0%)	14 (23.3%)	0.089
	Low	4	2 (50.0%)	0 (0.0%)	2 (50.0%)	0 (0.0%)	
	High	11	7 (63.6%)	0 (0.0%)	4 (36.4%)	0 (0.0%)	
Folate Folic Acid	Normal	14	5 (35.7%)	2 (14.3%)	2 (14.3%)	5 (35.7%)	0.069
	Low	1	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
	High	8	1 (12.5%)	1 (12.5%)	6 (75.0%)	0 (0.0%)	
Current medications Steroids	Yes	13	3 (23.1%)	3 (23.1%)	1 (7.7%)	6 (46.2%)	0.035 ^a
	No	79	31 (39.2%)	17 (21.5%)	20 (25.3%)	11 (13.9%)	
Current medications DMARDS	Yes	87	33 (37.9%)	20 (23.0%)	19 (21.8%)	15 (17.2%)	0.312
	No	5	1 (20.0%)	0 (0.0%)	2 (40.0%)	2 (40.0%)	
Current medications Biological	Yes	34	10 (29.4%)	8 (23.5%)	7 (20.6%)	9 (26.5%)	0.408
	No	58	24 (41.4%)	12 (20.7%)	14 (24.1%)	8 (13.8%)	

^asignificant at the 5% level based on the chi-square test.

RA, rheumatoid arthritis; DMARDS, Disease-modifying antirheumatic drugs; TSH, thyroid-stimulating hormone; CCP, cyclic citrullinated peptide; RF, rheumatoid factor; vit, vitamin

DISCUSSION

Our study demonstrated that a high proportion of patients with RA at XXX University Hospital (63%) were at risk of depression, based on PHQ9 scores. Notably, the same proportion was also at risk of anxiety, based on GAD7 scores. The risk of depression was significantly higher than that in a similar study conducted on RA patients at this University Hospital during the period 2008–2010 (18%) (Attar, 2014). Egypt and Slovakia reported a higher rate of symptoms of depression (66.2%, 73.2%, respectively) and anxiety (70%, 85.2%, respectively) than that found in this study (El-Miedany and El-Rasheed, 2002; Soósová et al., 2017). A lower prevalence of depression was noted in the United Kingdom (UK, 38.8%), Australia (40%), and the United States of America (USA, 18%) (Matcham et al., 2013; Murphy et al., 2012; Covic et al. 2006), while a lower prevalence of anxiety was noted in RA patients in the USA

(31%) and the UK (13.5%) (Covic et al., 2012; Murphy et al., 2012). This variation might be due to different factors and determinants, and particularly the different assessment tools for depression and anxiety and the varying ages of the subjects.

Moreover, the present study data were collected in the midst of the COVID-19 pandemic, which markedly increased people's mental distress and health issues. Interestingly, in our study the prevalence of anxiety and depression were the same, whereas in other countries, such as the USA and Egypt (El-Miedany and El-Rasheed, 2002; Murphy et al., 2012), anxiety was more common than depression among RA patients. Our results showed that the severity of depression and anxiety symptoms was directly associated with the severity of RA, level of pain, and lower quality of life. Our results agreed with the current literature that RA patients have a worse course of disease, greater level of pain, and lower quality of life (Kojima et al., 2009;

Ozçetin et al., 2007), although it is not well established whether the severity of pain worsens depression and anxiety symptoms, or vice versa (Covic et al. 2006). Statistical analysis showed no significant differences

between levels of depression and anxiety symptoms and socio-demographic factors, except for the association between the level of anxiety and age. Specifically, the older the RA patient, the higher was the level of anxiety. Similarly,

Table 9: Association between depression and clinical findings in RA patients

Variables	Total	Patient Health Questionnaire					p-value	
		Normal	Mild	Moderate	Moderately Severe	Severe		
Total	92	34 (37.0%)	25 (27.2%)	16 (17.4%)	9 (9.8%)	8 (8.7%)	-	
RF	Positive	34	12 (35.3%)	9 (26.5%)	6 (17.6%)	4 (11.8%)	3 (8.8%)	0.989
	Negative	57	22 (38.6%)	16 (28.1%)	9 (15.8%)	5 (8.8%)	5 (8.8%)	
Anti-CCP	Positive	50	17 (34.0%)	14 (28.0%)	9 (18.0%)	4 (8.0%)	6 (12.0%)	0.688
	Negative	33	16 (48.5%)	7 (21.2%)	5 (15.2%)	3 (9.1%)	2 (6.1%)	
Seropositivity	Seropositive	57	20 (35.1%)	15 (26.3%)	10 (17.5%)	6 (10.5%)	6 (10.5%)	0.914
	Seronegative	34	14 (41.2%)	10 (29.4%)	5 (14.7%)	3 (8.8%)	2 (5.9%)	
Vit-B12	Normal	49	21 (42.9%)	14 (28.6%)	7 (14.3%)	7 (14.3%)	0 (0.0%)	0.039 ^a
	Low	17	5 (29.4%)	5 (29.4%)	3 (17.6%)	1 (5.9%)	3 (17.6%)	
Vit-D	Normal	21	8 (38.1%)	5 (23.8%)	3 (14.3%)	3 (14.3%)	2 (9.5%)	0.898
	Low	68	26 (38.2%)	20 (29.4%)	12 (17.6%)	6 (8.8%)	4 (5.9%)	
TSH	Normal	60	24 (40.0%)	15 (25.0%)	10 (16.7%)	6 (10.0%)	5 (8.3%)	0.728
	Low	4	1 (25.0%)	2 (50.0%)	0 (0.0%)	1 (25.0%)	0 (0.0%)	
	High	11	3 (27.3%)	5 (45.5%)	2 (18.2%)	1 (9.1%)	0 (0.0%)	
Folic Acid	Normal	14	4 (28.6%)	5 (35.7%)	3 (21.4%)	2 (14.3%)	0 (0.0%)	0.813
	Low	1	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
	High	8	2 (25.0%)	2 (25.0%)	2 (25.0%)	2 (25.0%)	0 (0.0%)	
Current medications	Yes	13	3 (23.1%)	2 (15.4%)	3 (23.1%)	1 (7.7%)	4 (30.8%)	0.034 ^a
Steroids	No	79	31 (39.2%)	23 (29.1%)	13 (16.5%)	8 (10.1%)	4 (5.1%)	
Current medications	Yes	87	33 (37.9%)	23 (26.4%)	15 (17.2%)	8 (9.2%)	8 (9.2%)	0.777
DMARDS	No	5	1 (20.0%)	2 (40.0%)	1 (20.0%)	1 (20.0%)	0 (0.0%)	
Current medications	Yes	34	14 (41.2%)	9 (26.5%)	5 (14.7%)	3 (8.8%)	3 (8.8%)	0.969
Biological	No	58	20 (34.5%)	16 (27.6%)	11 (19.0%)	6 (10.3%)	5 (8.6%)	

^asignificant at the 5% level based on the chi-square test

RA, rheumatoid arthritis; DMARDS, Disease-modifying antirheumatic drugs; TSH, thyroid-stimulating hormone; CCP, cyclic citrullinated peptide; RF, rheumatoid factor; vit, vitamin

a previous meta-analysis demonstrated that socio-demographic factors play no role in the development of mental illness (Dickens et al., 2003). However, another meta-analysis found that the mean age was the main factor influencing the prevalence of depression among patients with RA (Matcham et al., 2013). Additionally, older patients are thought to be more prone to developing anxiety (Peterson et al., 2019). We found that older patients tend to have more severe anxiety symptoms, which might be due to the nature of the disease and the impaired coping mechanism of older individuals (Fragoulis et al., 2020). We found a similar proportion of RA patients with low vitamin B12 levels (25.8%) as that found in other studies (24% and 29%) (Segal et al., 2004; Vreugdenhil et al., 1990). Although both groups with low and normal levels of vitamin B12 showed a significant association with depression,

depression was less evident in patients with normal levels of vitamin B12 (57.2%) than in patients with low levels of vitamin B12 (70.6%). This supports the findings of previous studies of the effect of vitamin B12 on depression. Vitamin B12 is thought to help delay the onset of depression if used early in the course of the disease, and to improve the effect of antidepressants (Sangle et al., 2020).

A well-known side effect of steroid treatment is depression. In this study, a notable greater proportion of RA patients treated with steroids reported both depression and anxiety symptoms (77%) than did RA patients who did not use steroids. However, those who did not use steroids also included a high proportion of individuals with depression and anxiety (60.8% and 60.7%, respectively). Medicating with steroids is considered a significant predictor of depression in patients with RA (Lapčević et al.,

2017). The majority of patients responded favorably when offered a visit to a psychiatric clinic (56.5%). Of these, 78.8% had anxiety and 76.9% had depression. Therefore, we recommend that RA patients with symptoms of depression and/or anxiety be referred to a psychiatrist and that caution should be used when considering high doses of

standing disease. In addition, factors such as psychological treatments, antidepressant treatments, and medication adherence were not considered. These, in addition, the timing of the study (during the COVID-19 pandemic) may have affected the results. Moreover, a small number of our patients could not be reached as they could not be contacted.

CONCLUSION

Our study shows that RA is commonly comorbid with psychological struggles, such as depression and anxiety, which may worsen the course of the disease. In addition, this is worsened by steroid use and low vitamin B12 levels. Our study highlights the need to screen for psychological struggles in RA patients, and to offer them social support in order to improve their prognosis and quality of life.

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steroids. Additionally, large-scale prospective studies are needed to determine the type of association between depression and anxiety and RA, and whether treating psychological issues would alter the course of RA. The study had many limitations. These include the small sample size and the fact that the majority of the patients had long-

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