Prevalence of Generalized Anxiety Disorder in Patients with Rheumatoid Arthritis and its Relationship with Disease Activity

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ABSTRACT

Background: rheumatoid arthritis (RA) is a lifelong disease with a progressive disabling course and individuals with RA experience higher levels of psychological distress than general population. **Objective:** the objective of the present study was to assess the prevalence of generalized anxiety disorder (GAD) in RA patients and determine its relationship with disease activity. **Patients and Methods:** the study included 200 RA cases. Psychiatry examinations of all cases were performed according to Hamilton scale. Patients who suspected to have GAD were further assessed by the most recent diagnostic criteria for GAD in diagnostic and statistical manual of mental disorders fifth edition (DSM-5) and psychiatry assessment sheet (PAS). **Results:** the prevalence of GAD in RA cases was 38.5% (n=77) assessed by psychiatry assessment sheet (PAS). RA patients with GAD significantly showed higher disease activity measures than those without GAD (P value <0.001). It was found that GAD did not related to disease duration (r=0.617; p value >0.05) or RF positivity (r=0.058; p value >0.05). **Conclusion:** generalized anxiety disorder (GAD) is common to occur in RA cases. Disease activity was significantly higher in RA cases with GAD than RA cases without GAD. GAD was found to be not related to disease duration.

Keywords: Rheumatoid arthritis, generalized anxiety disorder.

INTRODUCTION

Rheumatoid arthritis (RA) is a systemic, chronic, and inflammatory disease with probable autoimmune etiology and predominant involvement of joints, characterized by symmetrical peripheral polyarthritis, resulting in joint deformity [1]. In addition to producing a chronic inflammatory state, the disease generally causes many harmful psychosocial consequences for patient [2]; also the patient with this chronic disease faces the course of which cannot be predicted and a painful progression marked with attacks [3].

Continuous pain, functional disability, tiredness, incapacity to work, economic limitations, and side effects of therapeutic drugs, which RA may bring about, can end up reducing these patients's quality of life [4]. In addition, psychiatric symptoms in RA patients increase the perception of pain, use of analgesics and work disability and lead to reduction in drug compliance [5].

One of the factors believed to play a role in the initiation, maintenance and exacerbation of RA is psychological stress. The diagnosis of RA may cause stress and uncertainty in patients and their relatives, also higher stress at the onset of the disease predicts worse disease prognosis [6].

It is hypothesized that chronic pain, joint deformities, loss of function and work disability lead to social stress and contribute to the development of psychiatric disorders in RA patients [7], also multiple lines of investigations suggest that stress plays a significant role in shaping the cause of inflammatory diseases such as RA; stress activates a cascade of neuro-humoral events many of which may be dys-regulated in RA patients, including aspects of the hypothalamic-pituitary-adrenal axis (HPA), the autonomic nervous system, and pro-inflammatory processes [8], so this implies that the endocrine stress response system could be a target for stress management interventions in patients with immune-mediated diseases such as RA [9].

People with RA tend to experience more anxiety and other emotional problems than other people in the general population, moreover, it is found that anxiety has a direct effect on pain and that effect was significantly higher than that of depression. Previous research has revealed that a frequent temporal sequence is anxiety first and then subsequently depression. Therefore, screening for symptoms of anxiety in persons with RA might facilitate early identification of depression and help to prevent future depressive episodes [10].

One of the most common types of anxiety disorders in RA is the generalized anxiety disorder (GAD) [11]. GAD is characterized by excessive anxiety and worry about a variety of

topics (such as health, work, family… etc.) occurring more days than not for at least six months and is accompanied by physical symptoms [12].

AIMS OF THE STUDY:

The aims of this study were to assess:

1. Prevalence of generalized anxiety disorder (GAD) in patients with RA using the Hamilton Anxiety rating scale (HAM-A), Diagnostic and Statistical Manual of Mental Disorders (DSM-5) diagnostic criteria for GAD and the clinical psychiatric assessment sheet (PAS)

2. The differences in disease activity parameters between RA patients with and without GAD.

PATIENTS AND METHODS:

Study design:

A descriptive cross-sectional study of RA patients.

Patients:

Two hundred patients with definite diagnosis of RA attending the outpatient clinic of the Physical Medicine, Rheumatology and Rehabilitation department, Sohag University Hospital, were included for this study. Collection of RA patients was done in a period of six months, and data analysis and explanation were done in another period of six months.

Inclusion criteria:

1. Age > 17 years.

2. Able and willing to give written informed consent and comply with the requirements of the study protocol.

3. Patients with RA diagnosed according to the European League against Rheumatism/American College of Rheumatology (EULAR/ACR 2010) [17] and/or the 1988 ACR classification criteria [18].

4. Symptoms of generalized anxiety disorder onset after RA.

Exclusion criteria:

1. Definite autoimmune rheumatic disease other than RA including systemic lupus erythematosus, mixed connective tissue disease, scleroderma, seronegative spondyloarthropathies and polymyositis... etc.

2. Prior history of or current inflammatory joint disease (e.g., gout).

3. Patients with fibromyalgia syndrome.

4. History of previous psychiatric disorders.

5. Chronic disorders other than RA (e.g. diabetes mellitus, chronic liver disease, chronic renal failure… etc).

Patients' recruitment & counseling

Patients were recruited from outpatient clinic of the Rheumatology and Rehabilitation Department, Sohag University.

Methods:

Following history taking, complete general and musculoskeletal examination of RA patients; RA patients were subjected to the following assessment tools:

1. Demographic data including, name, age, sex, job, marital status, education, disease duration and morning stiffness were recorded for every RA patient.

2. Rheumatoid factor (RF).

3. Erythrocyte sedimentation rate (ESR).

4. Visual Analogue Scale (VAS) [19].

5. DAS-28 [20]

6. Hamilton Anxiety Rating scale (HAM-A) [13,21] and HAMA score Arabic translation [22]

This scale consists of the following 14 rating items:

1. Anxious Worries, anticipation of the worst, fearful anticipation, irritability.

2. Tension Feelings of tension, fatigability, startle response, moved to tears easily, trembling, feelings of restlessness, inability to relax.

3. Fears of dark, of strangers, of being left alone, of animals, of traffic, of crowds.

4. Insomnia Difficulty in falling asleep, broken sleep, unsatisfying sleep and fatigue on waking, dreams, nightmares, night-terrors.

5. Intellectual (cognitive): Difficulty in concentration, poor memory.

6. Depressed Mood: Loss of interest, lack of pleasure in hobbies, depression, early waking, diurnal swing.

7. Somatic (muscular): Pains and aches, twitching, stiffness, myoclonic jerks, grinding of teeth, unsteady voice, increased muscular tone.

8. Somatic (sensory): Tinnitus, blurring of vision, hot and cold flushes, feelings of weakness, pricking sensation.

9. Cardiovascular Symptoms: Tachycardia, palpitations, pain in chest, throbbing of vessels, fainting feelings, missing beat.

10. Respiratory Symptoms: Pressure or constriction in chest, choking feelings, sighing, dyspnea.

11. Gastrointestinal Symptoms: Difficulty in swallowing, wind, abdominal pain, burning sensations, abdominal fullness, nausea, vomiting, borborygmi, looseness of bowels, loss of weight, constipation.

12. Genitourinary Symptoms: Frequency of

micturation, urgency of micturation, amenorrhea, menorrhagia, development of frigidity, premature ejaculation, loss of libido, impotence.

13. Autonomic Symptoms: Dry mouth, flushing, pallor, tendency to sweat, giddiness, tension headache, raising of hair.

14. Behavior at Interview: Fidgeting, restlessness or pacing, tremor of hands, furrowed brow, strained face, sighing or rapid respiration, facial pallor, swallowing, belching, brisk tendon jerks, dilated pupils, exophthalmos.

Each of these 14 items is scored as follows: NONE = 0, MILD = 1, MODERATE = 2, SEVERE = 3, SEVERE, GROSSLY DISABLING = 4

This calculation will yield a comprehensive score in the range of 0 to 56. It has been predetermined that the results of the evaluation can be interpreted as follows. A score of 17 or less indicates mild anxiety severity. A score from 18 to 24 indicates mild to moderate anxiety severity. Lastly, a score of 25 to 30 indicates a moderate to severe anxiety severity.

7. Diagnostic and Statistical Manual of Mental Disorders, 5th Ed. (DSM-5) diagnostic criteria for GAD [14-16] These include:

A. Excessive anxiety and worry (apprehensive expectation), occurring more days than not for at least 6 months, about a number of events or activities (such as work or school performance).

B. The individual finds it difficult to control the worry.

C. The anxiety and worry are associated with three (or more) of the following six symptoms (with at least some symptoms having been present for more days than not for the past 6 months):

1. Restlessness or feeling keyed up or on edge.
2. Being easily fatigued.
3. Difficulty concentrating or mind going blank.
4. Irritability.
5. Muscle tension.
6. Sleep disturbance (difficulty falling or staying asleep, or restless, unsatisfying sleep).

D. The anxiety, worry, or physical symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

E. The disturbance is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition (e.g., hyperthyroidism).

F. The disturbance is not better explained by another mental disorder (e.g., anxiety or worry about having panic attacks in panic disorder, negative evaluation in social anxiety disorder [social phobia], contamination or other obsessions in obsessive-compulsive disorder, separation from attachment figures in separation anxiety disorder, reminders of traumatic events in posttraumatic stress disorder, gaining weight in anorexia nervosa, physical complaints in somatic symptom disorder, perceived appearance flaws in body dysmorphic disorder, having a serious illness anxiety disorder, or the content of delusional beliefs in schizophrenia or delusional disorder).

8. Psychiatry assessment sheet for patient assessment and diagnosis:

It is obtained from outpatient clinic of Psychiatry Department, Sohag University.

The scales included in this study were carefully explained to   illiterate patients in order to answer accurately on each item.

The patients in this study were informed about the study, and their consents were obtained.

Analysis:

Data was calculated and analyzed using IBM-SPSS, version 22 software.

RESULTS

Demographic data in patients: Two hundred patients were included in this study and the age distribution of the patients ranged between 18 and 70 years with average of 42.34±11.99 years. One hundred and sixty six of patients were females in a percent of 83% and thirty four were males in a percent of 17%. The disease duration ranged from 2 months up to 35 years, which was reflected in the very high standard deviation (6.2 years) compared to the mean (7.67 years). The classification of patients according to disease duration was as follows: five (2.5%) of patients were very early cases, 38 (19.0%) were early cases, 157(78.5%) were established cases

Table (1) shows evaluation of disease activity according to morning stiffness ranged from 0 to 150 minutes with average of 36.98±36.69, visual analogue scale (VAS) ranged from 0 to 100 with average of 29.43±28.06, number of swollen joints ranged from 0 to 8 with average of 1.50±1.97, number of tender joints ranged from 0 to 10 with average of 2.43±2.81.

The value of rheumatoid factor (RF) ranged from 4.8 to 2048 IU/ml with average of 213.46±337.69 and the value of ESR ranged

from 9 to 110 with average 35.43± 19.91 mm/hr. Concerning rheumatoid factor, 145 (72.5%) were RF +ve & the remaining 55 of patients (27.5%) were RF –ve. Concerning ESR 98 of patients (49.0%) were normal while in the other 102 patients (51.0%) ESR was raised. DAS-28 ranged between 1.82 and 6.07 with average of 3.69±1.22. Disease activity measured by DAS-28 is shown in the following table as follows: 85 of patients (42.5%) had mild disease activity, another 85 (42.5%) of patients had moderate disease activity and the remaining 30 (15.0%) had high disease activity.

Concerning Hamilton score for anxiety it ranged from 0 to 35 with average of 13.28±9.28. The prevalence and degrees of anxiety by Hamilton score was as follows: 124(62.0%) of patients considerably suspected to have mild anxiety, 46 cases (23.0%) have moderate anxiety, 28 cases (14.0%) have severe anxiety and 2 cases (1.0%) have very severe anxiety.

As regards the correlation between Hamilton scale, age, disease duration, and measures of disease activity in RA patients: there was no significant correlation between Hamilton scale and; age, disease duration, RF positivity (p value > 0.05). On the other hand, there was a very highly significant correlation between Hamilton scale and morning stiffness, VAS, number of swollen joints, number of tender joints, ESR and DAS-28 (p value < 0.001) (Table 2).

We found that there was no significant difference in anxiety measured by Hamilton scale between male and female gender (p value > 0.05). Also, there was no significant difference in Hamilton scale between RF positive and RF negative cases (p value > 0.05). On the other hand, the mean Hamilton scale among patients with raised ESR was 19.55±7.67, which was much higher than that among patients with normal ESR (6.76±5.58); the p value was highly significant (<0.001).

Comparing Hamilton score with disease activity using DAS28 showed that the mean Hamilton score raised from 4.61±3.1 among low disease activity patients, to 17.39±6.02 among moderate disease activity patients, to 26.2±3.99 among those with high disease activity. The difference was, highly significant.

All of the 85 patients with mild disease activity had suspected mild anxiety, patients with

moderate disease activity had suspected anxiety as follows: 38(44.7%) of them had suspected mild anxiety, 41 (48.2%) of them had suspected moderate anxiety and 6 (7.1%) of them had suspected severe anxiety. Furthermore, cases with high disease activity had suspected anxiety as follows: one of them (3.3%) had suspected mild anxiety, 5 (16.7%) had suspected moderate anxiety, 22 (73.3%) had suspected severe anxiety and 2 (6.7%) had suspected very severe anxiety (Figure 1).

The prevalence of generalized anxiety disorder (GAD) among patients with RA selected assessed by DSM diagnostic criteria for GAD fifth edition (DSM-5) was as follows: patients that didn't met the criteria for GAD 117 (58.5%) and patients that met the diagnostic criteria for GAD 83 (41.5%).

Table 3 shows that there is a significant difference in disease activity measures between RA patients with and without generalized anxiety disorder assessed by DSM-5 as follows: morning stiffness, VAS, number of tender joints, number of swollen joints, ESR and DAS-28 are higher in RA patients with positive generalized anxiety disorder compared with those without (p value < 0.001).

There was a significant difference in RA patients with positive generalized anxiety disorder assessed by DSM-5 and those assessed by Hamilton scale as follows: Two hundred RA patients have suspected anxiety assessed by Hamilton scale compared with eighty three of those RA patients have suspected generalized anxiety disorder by DSM-5 (p value < 0.001).

Concerning the prevalence of generalized anxiety disorder assessed by psychiatry assessment sheet (PAS), 77 (38.5%) of two hundred RA patients approved to have generalized anxiety disorder (p value < 0.001).

Table 4 shows that there are significant differences in measures of disease activity as regards morning stiffness, VAS, number of tender joints, number of swollen joints, ESR and DAS-28 between RA patients with and without GAD assessed by psychiatry assessment sheet (p value < 0.001). As regards sex, age, disease duration and RF positivity there is no statistical difference (p value > 0.05) between RA patients with and without GAD assessed by psychiatry assessment sheet.

DISCUSSION

Having a chronic illness like RA can be emotionally challenging. In fact, when patients diagnosed with RA, the first thing they may find themselves doing is dealing with the

powerful feelings that surface, including anxiety, uncertainty, and fear. After overcoming the initial reaction, the daily challenges posed by RA increase the risk for emotional problems like depression, anxiety and stress. It has been shown that RA cases either quit or change their jobs in a 2-year period with a rate of 33 and 16%, respectively. The chronicity and clinical fluctuations of the disease as well as the ever-present possibility of patient's suffering pain are the possible causes of psychiatric disorders in RA [23].

Most studies of disease activity in RA have focused on clinical pain severity while recent studies reported a complex relation between pain, inflammation and psychological distress in RA patients [24].

In a study done by Murphy and her co-investigators about the prevalence of anxiety and depression in patients with chronic arthritis like RA it was found that more than one-third of the study participants had at least one of two mental health conditions: anxiety and depression. Anxiety was far more common than depression in a proportion of twice as high as depression, however according to the researchers this was un-expected as there is so much more attention paid to depression [25]. Radanov et al. [26,27] found that persons with RA exhibited average trait anxiety scores, which were similar to the normative data for the general population.

These conflicting results regarding the prevalence of anxiety in RA warrant further investigation. Most studies had investigated prevalence of anxiety disorders in general in RA; also these studies were either small-scale or used female patients predominantly [28].

In our study we are focused on prevalence of generalized anxiety disorder (GAD) - as the commonest current anxiety disorder as reported by Lok et al. [28] in RA patients and its relationship with parameters of disease activity. The differences in assessment scales create difficulties in comparing results across studies [29].

In our study we tried to overcome this problem and we used the most commonly accepted diagnostic gold standard and the most recent one which is the diagnostic and statistical manual of mental disorders 5th edition, together with Hamilton scale for anxiety (HAM-A).

Although the HAM-A remains widely used as an outcome measure in clinical trials, it has been criticized for its sometimes poor ability to discriminate between anxiolytic and antidepressant effects, and somatic anxiety versus somatic side effects. The HAM-A does not provide any standardized probe questions. Despite this, the reported levels of interrater reliability for the scale appear to be acceptable; also it covers many of the features of GAD and can be helpful also in assessing its severity [30]

Two hundred RA patients - diagnosed according to the 1987 American college of Rheumatology Classification Criteria (ACR) [18], and/or (EULAR/ACR 2010) classification criteria [17] - were included in this study. One hundred and sixty-six (83%) were females and the remaining 34 (17%) were males, age of the patients ranged between 18 and 70 years with average of 42.34±11.987 years. The patients were assessed by Hamilton anxiety rating scale (HAM-A) [13] and patients suspected to have anxiety were further assessed by the most recent diagnostic criteria for GAD by diagnostic and statistical manual of mental disorders fifth edition (DSM-5) [14-16] and psychiatric assessment sheet.

The results showed that prevalence of GAD by Hamilton scale was 62% mild anxiety 37% moderate to severe anxiety and 1% very severe anxiety this differed from a study of prevalence of GAD (by Hamilton) in RA patients done by eHealthMe [31] that showed 100.00% of cases had moderate anxiety (by Hamilton). Total prevalence of GAD ranged from 38.5% (n= 77) by psychiatry assessment sheet and 41.5% (n= 83) by DSM-5. This prevalence was consistent with other studies despite different assessment measures [3,32,33]. However, this prevalence was lower than the following studies [4,5,34], this may be due to in these studies they found a co-morbid association between anxiety and depression (i.e. overlap).

This prevalence found to be higher than other studies [10,25,28,35,36]. This difference in prevalence may be due to the different assessment measures and scales used in our study using the most recent DSM-5 criteria and psychiatry assessment sheet (PAS) together with Hamilton scale. The number of the participants may be another factor. Also the low educational level in our region and our patients may be another factor. It has been reported by Treharne [23] that low socioeconomic status is associated with poor health in normal individuals and RA cases, so this may be another possible factor responsible for higher prevalence of anxiety in our study.

It has been reported that there is no significant relation between anxiety and disease duration in RA [4,24,37]. Our study agreed with these results (r=0.013; p value > 0.05). However, this finding appears to be inconsistent with previous reports that showed a decrease in anxiety over the first few years of having RA [35,36,38-42]. Odegard *et al*. [3] found that anxiety was strongly associated with the course of pain for patients with recent onset RA.

Another finding in our study is that there was a very significant prolongation in morning stiffness, higher VAS, higher number of swollen joints, higher number of tender joints, higher ESR and DAS-28 among patients that proved to have GAD (by Hamilton, DSM-5 and psychiatric assessment sheet) and those without GAD. This finding was observed in the following studies except for ESR [4,24,33,37]. Also Kekow *et al*. [4] found that among moderate to severe active early RA patients, clinical remission reduces symptoms of anxiety. These correlations may reflect that anxiety is related to observable features of the disease such as tender and swollen joints or the underlying disease process.

In the previous studies ESR didn't show significant difference in patients with and without anxiety, this lack of association didn't seen in our study as ESR was found to be significantly different in patients proved to have GAD (by Hamilton, DSM-5 and psychiatric assessment sheet) and patients without GAD (p value < 0.001) and this supported the suggestion that GAD is associated with the underlying pathological process in RA as reported by [35,43-48] . Also it has been found that psychological interventions, such as multimodal cognitive behavioral therapy (CBT), biofeedback and stress management training, have generally led to modest improvements in psychological and physical functioning in patients with RA and GAD, with similar effects on biological measures of disease, such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) [45,46,49] and significant reduction in anxiety [9].

This was in contrast with Mak *et al*. [50] who found that the lack of inflammatory parameters (ESR, CRP and RF positivity) was found in RA as well as in systemic lupus erythromatous and this weakens the assumption that anxiety is associated with the underlying pathological disease process.

Tamiya [51] and Vaeroy [52] found a positive relation between pain in RA and anxiety, Tamiya [51] found 30% of the variance in pain explained by anxiety. In our study we found that there was correlation between pain (VAS) and GAD in RA patients and this correlation was highly significant (r =0.841 and p value < 0.001).

In our study we found that there was no significant difference in terms of age, sex, rheumatoid factor positivity in patients with and without GAD (p value > 0.05) this finding was consistent with other studies [4,24,35-37].

The last assessment of patients by psychiatric assessment sheet helped us to identify patients at high risk. Patients with financial difficulties and poorer social interactions were found to be at risk for anxiety, however, because a causal relationship cannot be implied from a statistical association, this could arise from various mechanisms and this was consistent with Soderlin *et al*. [53] and Lok *et al*. [28].

It was reported that usage of corticosteroid, especially high-dose and long-term [54] and NSAIDs [55] led to psychiatric side effects. On the other hand, corticosteroid and DMARDs used in RA cases did not influence anxiety and had recovering effects on physical conditions [56]. In our study patients were under DMARDs therapy either monotherapy or in combination and some combined with low dose corticosteroid or leflunomide.

In conclusion: generalized anxiety disorder (GAD) is common to occur in RA patients. After assessment of associated factors in RA its relation with disease activity remained statistically significant from patients without GAD. The identification of factors associated with psychiatric disorders in RA patients may contribute to the development of possible preventive measures.

RECOMMENDATIONS

Rheumatologists have to be aware of the social and family background of patients, and provide assistance to patients who are at risk. Patients should also be encouraged to participate in social activities and play an active role in self-help groups, which may help to enhance their sense of perceived social support and degree of social interaction.

The investigation of anxiety as well as a multidisciplinary treatment approach and follow-up in RA patients may be recommended. Also early referral to a multidisciplinary psychiatric team may help to

improve the outcome of psychiatric disorders in RA patients.

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Table 1: Clinical evaluation of disease activity

	Morning stiffness (Min)	VAS (0-100)	Swollen joints	Tender joints
Mean	36.98	29.43	1.50	2.43
Median	20.00	20.00	0.00	1.50
Std. Deviation	36.69	28.06	1.97	2.81
Minimum	0	0	0	0
Maximum	150	100	8	10

Table 2: Correlations between Hamilton score and each of age, disease duration and severity of RA patients

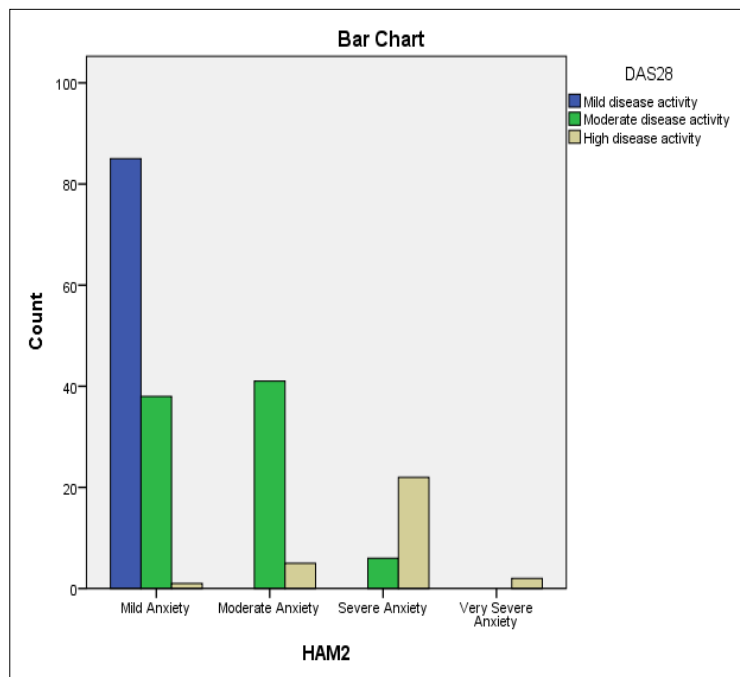|	Pearson correlation (r)	P value
Age (years)	0.013	0.858
Disease duration (years)	0.036	0.617
Morning stiffness (minutes)	0.772	<0.001
VAS (0-100)	0.841	<0.001
Swollen joints (number)	0.751	<0.001
Tender joints	0.816	<0.001
RF (IU/mL)	0.058	0.416
ESR (mm/hr)	0.752	<0.001
DAS28	0.904	<0.001

Figure 1: Relation between disease activity and degree of anxiety

Table 3: Comparison of disease activity measures between male and female RA patients with and without generalized anxiety disorder assessed by DSM-5

		DSM-5 Patients without Anxiety	Patients with Anxiety	Chi square*/ t test** MW test***	P value
Sex	Male	19	15	0.116*	0.734 (NS)
	Female	98	68		
Age (mean±SD)		42.52±11.49	42.07±12.72	0.260**	0.795 (NS)
Disease duration (years)		7.92±5.91	7.623±6.60	4418.5***	0.277 (NS)
Duration of RA	Very early RA	1	4	3.393*	0.183 (NS)
	Early RA	24	14		
	Established RA	92	65		
Morning stiffness (min)		16.79±25.47	65.42±30.80	1036.0***	**<0.001 (HS)**
VAS (0-100 scale)		12.39±16.43	53.43±23.05	791.0***	**<0.001 (HS)**
No. of tender joints		0.72±1.14	4.83±2.70	1136.0***	**<0.001 (HS)**
No. of swollen joints		0.39±0.80	3.05±2.08	792.5***	**<0.001 (HS)**
RF		183.03±34.96	256.35±36.81	4230.5***	0.120 (NS)
RF positivity	Negative RF	34	21	0.344*	0.558 (NS)
	Positive RF	83	62		
ESR		24.79±1.41	50.41±19.71	10.642**	**<0.001 (HS)**
ESR	Normal	87	11	77.550*	**<0.001 (HS)**
	Raised	30	72		
DAS-28		2.91±0.78	4.79±0.81	16.527**	**<0.001 (HS)**
DAS-28 group	Mild disease activity	81	4	98.817*	**<0.001 (HS)**
	Moderate	36	49		
	Severe	0	30		
Hamilton Score(anxiety)		6.82±1.63	22.39±5.95	20.809**	**<0.001 (HS)**
Anxiety by HAM	Mild anxiety	117	7	172.794*	**<0.001 (HS)**
	Moderate	0	46		
	Severe	0	28		
	Very severe	0	2		
Psychiatry case sheet	Negative anxiety	117	6	176.491*	**<0.001 (HS)**
	Positive anxiety	0	77		
Total		117	83		200

MW: Mann Whitney test, used instead of t test if the data are not normally distributed

Table 4: Comparison between Psychiatry assessment sheet positive and negative cases for anxiety

		Psychiatry Assessment Sheet Patients without Anxiety	Patients with Anxiety	Chi square*/ t test** MW test***	P value
Sex	Male	23	11	0.654*	0.419 (NS)
	Female	100	66		
Age (mean±SD)		42.41±11.74	42.21±12.45	0.118**	0.906 (NS)
Disease duration (years)		7.92±5.94	7.49±6.62	44.83.5***	0.526 (NS)
Morning stiffness (min)		16.63±24.87	69.48±28.13	784.0***	**<0.001 (HS)**
VAS (0-100 scale)		12.64±16.26	56.23±21.28	570.0***	**<0.001 (HS)**
No. of tender joints		0.73±1.15	5.13±2.54	497.5***	**<0.001 (HS)**
No. of swollen joints		0.43±0.93	3.19±1.99	920.5***	**<0.001 (HS)**
RF		184.67±308.29	259.46±377.54	4003.0***	0.065 (NS)
ESR		24.54±9.47	52.82±18.10	12.258**	**<0.001 (HS)**
ESR	Normal	92	6	85.076*	**<0.001 (HS)**
	Raised	31	71		
DAS-28		2.91±0.80	4.93±0.58	20.872**	**<0.001 (HS)**
Hamilton Score(anxiety)		6.79±4.61	23.65±3.79	25.500***	**<0.001 (HS)**
Total		123	77	-	-

MW: Mann Whitney test, used instead of t test if the data are not normally distributed