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Anxiety and Depression in Iraqi Rheumatoid Arthritis Patients Treated with Anti- Tumor Necrosis Factor and Their Relationship with Disease Activity

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Abstract

Rheumatoid arthritis is a chronic systemic autoimmune inflammatory disease, characterized by progressive and destructive polyarthritis which affects the joints and other body systems. Depression and anxiety are highly prevalent in RA and impairs the quality of life in RA cases. To evaluate anxiety and depression in RA patients treated with Anti-Tumor Necrosis Factor and their relationship with disease activity. A case-control study was conducted at the rheumatology unit, Baghdad teaching hospital in Medical City during the period from October 2017 to May 2018. The study included 100 RA treated with Anti-Tumor Necrosis Factor and 100 controls. Data were collected using a pre-constructed data collection sheet. The mean age for patients and control was 52.6±7.8 and 53.7±8.2 years respectively. Depression and anxiety were found in 16% and 48% of patients with RA respectively, while seen in 10% and 43% of controls. In RA patients treated with Anti-Tumor Necrosis Factor, depression and anxiety were significantly correlated with disease duration, disease activity, and duration of biological treatment.

Depression and anxiety were less frequent in RA patients treated with Anti-Tumor Necrosis Factor drugs. The coexistence of depression and or anxiety with RA negatively impact the scores of disease activity in RA and they were associated with poor response to Anti-Tumor Necrosis Factor drugs.

Keywords: Rheumatoid Arthritis, Depression; Anxiety; Anti-Tumor Necrosis Factor; Baghdad

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Introduction

Rheumatoid arthritis (RA) is a systemic chronic inflammatory disease of unknown etiology that is characterized by a progressive and destructive polyarthritis in association with serological evidence of auto-reactivity. The progression of this disease can be slowed down with adequate medical control [1]. RA affects approximately 0.5-1% of the population worldwide, it is more common in female than male (female: male 3:1), with peak incidence 50-70 [2]. The prevalence is variable in different ethnic groups as the higher incidence and prevalence of RA in Finland, while low prevalence in West Africa [3]. The prevalence in Iraq is 1% in those aged 16 years or more compared to that recorded in Northern Europe [4]. Attaining remission in RA patients will prevent joint destruction (or at least progression of joint damage), optimize physical function, improve quality of life and work capacity, and reduce comorbidity risks. So the goal of RA treatment is stringent disease control to improve the outcomes [5]. The initial therapy of RA usually consists of mono-therapy with conventional synthetic disease-modifying anti-rheumatic drugs (cs DMARD), considering methotrexate is the first preferable choice (unless there is a contraindication or early to intolerance to it), if treatment target not achieved, a subsequent switching to (or adding of) another csDMARD should be considered (with or without short term glucocorticoids). Furthermore, if the treatment with using csDMARD alone failed, an addition of a biological DMARD or a target synthetic DMARD (tsDMARD) as tofacitinib will often be the next treatment step (6). The biological DMARD including Anti-Tumor Necrosis Factor that including Adalimumab, Etanercept, Cetrolizumabpegol, Golimumab, and Infliximab. Infliximab, Adalimumab, and Golimumab all are Immunoglobulin G1 (IgG1) monoclonal antibodies. The Infliximab is a mouse/human chimeric monoclonal antibody but Adalimumab and Golimumab are fully human. While the etanercept is a genetically engineered fusion protein composed of 2 soluble extracellular portions of human TNF receptor 2 fused to the Fc portion of human IgG1 [6]. Other are Abatacept (a costimulation inhibitor), and Tocilizumab (an IL-6 blocker) [7]. Besides, Rituximab: is a chimeric mouse /human monoclonal antibody that direct against the CD20 molecule on the surface of B cells that express this marker, and as a sequence depletes them [8].

The depression define as a part of normal experience to feel unhappy during time of adversity, while depressive disorders (unipolar

depression) are mental illness characterized by a profound and persistent feeling of sadness or despair and/or loss of interest in things that were once pleasurable for at least 2 weeks [9]. The anxiety defined as a feeling of dread and accompanied by somatic signs that indicate a hyperactive autonomic nervous system. Anxiety is a response to a threat that is unknown, vague, or conflict. Anxiety disorders include disorders that share features of excessive fear and anxiety and related behavioral disturbances [10]. Fear is the emotional response to real or perceived imminent threat, whereas anxiety is anticipation of future threat. Obviously, these two states overlap, but they also differ, with fear more often associated with surges of autonomic arousal necessary for fight or flight, thoughts of immediate danger, and escape behaviors, and anxiety more often associated with muscle tension and vigilance in preparation for future danger and cautious or avoidant behaviors [10]. The presence of psychiatric disorders in RA cases alters the progress of the disease and adaptation to the treatment whereas the improvement of the psychiatric disorders increases success of the RA treatment [7-10]. The effect of Anti-Tumor Necrosis Factor treatment on depression and anxiety in patients with RA were improved in association with improvements of clinical activity, while other studies showed no association between them. None of the studies were able to determine whether changes in depression occur independent of or prior to any changes in markers of clinical disease activity [11].

Methods

Study Design and Setting

This was a case- control study conducted at the rheumatology unit, Baghdad teaching hospital in Medical City during the period from October 2017 to May 2018.

Patients Consent

Prior to data collection, a signed consent from each of the participant was obtained after explaining the purpose of the study and ensuring privacy of the data.

Patients Collection

A total of 100 Iraqi patients (84 female and 16 male) diagnosed with RA (by consultant rheumatologists) after fulfilling the 2010 ACR/EULAR classification criteria for rheumatoid arthritis who attended Rheumatology unit in Baghdad teaching hospital and met the inclusion criteria were enrolled in the study.

Control

There were 100 healthy controls (83 female and 17 male) matched for age and sex enrolled in the study. Those were collected in the hospital as relatives of patients, visitors and health workers.

Inclusion Criteria

Patients who diagnosed with RA with disease onset after the age of 16 years regardless the disease duration, were evaluated for 2010 ACR /EULAR Classification Criteria for RA, all patient were on regular treatment included conventional disease modifying anti- rheumatic drug and biological drugs for 6 months prior to study entry.

Exclusion Criteria

- Those patients with major changes in their DMARD therapy during the previous six months
- Those with known diagnosis of anxiety-depressive syndrome
- Fibromyalgia
- Treated with anti-depressants drugs

Exclusion done by full history and examination. Psychiatric disorders were excluded in suspected patients with psychological problems by full assessment by consultant psychologist in psychological unit in Baghdad teaching hospital, fibromyalgia were excluded by applying modified 2010/2011 ACR Fibromyalgia Diagnostic Criteria.

Data Collection

Data were collected using a data collection sheet containing questionnaires for the patients and controls. The questionnaires included general demographic data: name, age, sex, weight, height, BMI, marital status, education level, and smoking.

Data for RA evaluation included disease duration, RF and ACPA were recorded from patient medical files. Disease activity was measured using Clinical Disease Activity Index (CDAI).

The clinical disease activity index (CDAI) score was developed for following patients with rheumatoid arthritis, composed from taking the number of tender joints (0-28), number of swollen joints (0-28), patient global health assessment (0=best to 10=worst) and care provider global health assessment (0=best to10=worst).

It done through the following equation: CDAI=TJC +SJC+PaGH+PrGH

Score interpretation as remission if between (0-2.8), low activity (2.9-10), moderate activity (10.1-22) and high activity (22.1-76). **Depression:** Depression was assessed with the PHQ-9. Each of the nine PHQ depression items corresponds to one of the DSM-IV Diagnostic Criterion A symptoms for major depressive disorder. Subjects were asked how often, over the last 2 weeks, they have been bothered by each of the depressive symptoms. Response options are “not at all”, “several days”, “more than half the days”, and “nearly every day”, scored as 0, 1, 2 and 3, respectively. PHQ-9 scores range from 0 to 27, with scores of≥5, ≥10,≥15, representing mild, moderate and severe levels of depression severity .

Anxiety: Anxiety was assessed with the Zung anxiety scale which assess 20 statements, rating each item with 1(none or little of the time), 2 (some of the time), 3 (good part of the time) and 4 (most or all of the time).

The total raw scores range from 20-80 with scores 20-44 normal range, 45-59 mild to moderate anxiety levels, 60-74 marked to severe anxiety levels and 75-80 extreme anxiety levels.

Statistical Analysis

Data of RA patients and controls were entered and analyzed using the statistical package for social sciences (SPSS) version 25. Descriptive statistics presented as mean, standard deviation, range, frequencies and proportions. All continuous variables were tested for statistical normal distribution using histogram and normal distribution curve. Statistical tests applied according to the type of variables; Student’s t test for two independent samples was used to compare two means of a continuous variable. Chi-square and Fisher’s exact (when chi-square inapplicable) tests used alternatively to compare frequencies. Bivariate Pearson’s and Spearman’s correlation tests and logistic regression curve estimation were used to assess the correlations. Correlation coefficient (R) is an indicator of the strength and direction of correlation; its value ranged zero (complete no correlation) to one (perfect correlation) the higher R

value close to one indicated stronger correlation, the positive (no sign) R value indicated a direct (positive) correlation and the negative signed R indicated an inverse correlation. Level of significance of ≤ 0.05 was considered as significant difference or correlation.

Results

The demographic characteristics of the studied groups are shown in Table 1, without any statistically significant differences. The clinical and disease related characteristics of the RA patients revealed that the disease duration ranged 1.5 to 18 years with a mean of (7.2 ± 4.0) years, on the other hand, the mean duration of using biological therapy was 1.9 ± 1.0 years ranging 6 months to 4 years (Table 2).

The results of investigations and testing of the patients regarding the RF factor, ACPA and ESR are demonstrated in Table 3, whereas 79% of patients were RF positive, and 80% were ACPA positive. Almost all of RA patients used DMARDS (99%), MTX used by (87%), steroid (43%), and other medication used were less frequent including Sufasalazine (9%), Azathioprine (3%). Leflunomide (2%) and only one patient used HCQ, but the patients used multiple medication were common (Table 4). The mean CDAI of RA patients was 14.0 ± 4.2 (range: 5-28) and when the patients categorized according to their CDAI levels it had been found that 20% at low disease activity, 79% at moderate and only one patient at high disease activity (Table 5 and Figure 1).

According to PHQ9 scores, depression was reported in 16% of RA patients, of them 9% had mild major depression and 7% with moderate major depression. Among controls, depression was reported in 10% subjects of them 7% subjects with mild major depression and 3% subjects had moderate major depression, meanwhile the difference between both groups was neither significant in the presence of depression in general nor the severity of depression in both comparisons (P>0.05) (Table 6).

Table 1: Demographic characteristics of the studied groups.

		Group				P value
		RA patients (n= 100)		Controls (n= 100)		
		No.	%	No.	%	
Age (year)*	≤ 40	9	9.0	6	6.0	0.71
	41 - 50	35	35.0	31	31.0	
	51 - 60	34	34.0	40	40.0	
	> 60	22	22.0	23	23.0	
	Mean ± SD	52.6 ± 7.8		53.7 ± 8.2		0.36
Gender	Male	16	16.0	16	16.0	0.22
	Female	84	84.0	84	84.0	
Marital status	Single	11	11.0	10	10.0	0.11
	Married	78	78.0	81	81.0	
	Divorced/Widow	11	11.0	9	9.0	
Education	Uneducated	32	32.0	25	25.0	0.93
	Primary	24	24.0	19	19.0	
	Secondary	29	29.0	34	34.0	
	College/higher	15	15.0	22	22.0	
Smoking	Current/ex-smoker	19	19.0	15	15.0	0.45
	Non-smoker	81	81.0	85	85.0	
	Smoking amount (Pack year) mean ± SD (Range)	2.1 ± 1.0 (1-4)		1.7 ± 0.8 (1-3)		0.23
BMI category*	Normal	17	17.0	25	25.0	0.26
	Overweight	52	52.0	52	52.0	
	Obese	31	31.0	23	23.0	
	Mean ± SD	28.6 ± 4.3		27.8 ± 4.4		0.16
Diabetes mellitus	Yes	27	27.0	24	24.0	0.63
	No	73	73.0	76	76.0	
Hypertension	Yes	35	35.0	34	34.0	0.88
	No	65	65.0	66	66.0	
Other	Yes	19	19.0	22	22.0	0.60
	No	81	81.0	78	78.0	

Table 2: Distribution of duration of RA and biological therapy use of RA patients.

		No.
Disease duration (year)	Mean±SD	7.2± 4.0
	Range	1.5-18
Duration of biological therapy(year)	Mean±SD	1.9± 1.0
	Range	0.5-4.0

Table 3: Distribution of RF positive, ACPA Positive and ESR level of RA patients.

Parameter		Value
RF Positive n(%)		79(79.0)
ACPA Positive n(%)		80(80.0)
ESR mm/hr	Mean±SD	24.6± 10.2
	Range	6.0–60.0

Where: RF= Rheumatoid factor; ACPA= Anti-citrullinated peptide antibody

Table 4: Distribution of Medications used by RA patients.

Medication used	No.	%
DMARDS	99	99.0
MTX	87	87.0
Steroid	43	43.0
Sufasalazine	9	9.0
Azathioprine	3	3.0
Leflunomide	2	2.0
HCQ	1	1.0

Where: DMARD=Disease modifying antirheumatic drug; MTX=methotrexate; HCQ=hydroxychloroquine

Table 5: Distribution of CDAI levels of RA patients.

CDAI	Mean±SD*	14.0± 4.2
	Range	5-28
Disease activity category		
Low n(%)	20(20.0)	
Moderate n(%)	79(79.0)	
High n(%)	1(1.0)	
Total	100(100.0)	

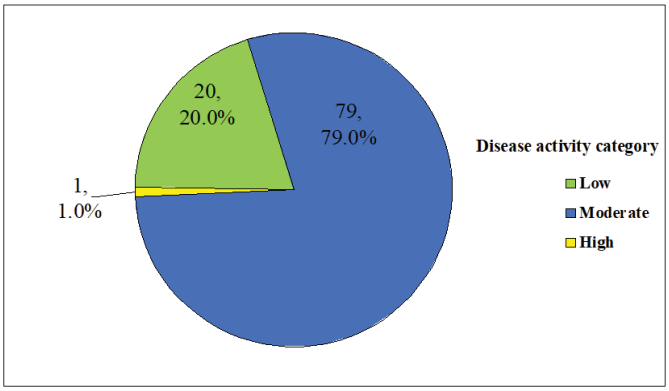

Figure 1: CDAI levels according to activity cutoff points of RA patients.

Table 6: Depression and Anxiety status and levels of RA patients and controls.

		Group				P Value
		RA patients (n= 100)		Control (n= 100)		
		No.	%	No.	%	
Depression	Yes	16	16.0	10	10.0	0.207
	No	84	84.0	90	90.0	
Depression severity	None	84	84.0	90	90.0	0.358
	Mild major depression	9	9.0	7	7.0	
	Moderate major depression	7	7.0	3	3.0	
Anxiety	Yes	48	48.0	43	43.0	0.478
	No	52	52.0	57	57.0	
Anxiety Level	None	52	52.0	57	57.0	0.691
	Middle	42	42.0	39	39.0	
	High	6	6.0	4	4.0	
Depression/Anxiety		55	55.0	44	44.0	0.12

Table 7: Comparison of mean total PHQ9 and anxiety scores of RA patients and controls.

Score		Group		P value
		RA patients (n= 100)	Control (n= 100)	
Total PHQ9 score	Mean±SD	8.08± 3.57	6.56± 3.60	0.003
	Range	1.0–17.0	1.0–15.0	
Anxiety score	Mean±SD	35.88± 6.64	33.62± 5.98	0.012
	Range	22.0–55.0	24.0–52.0	

According to the total anxiety score cutoff points, 48 RA patients and 43 controls had anxiety, on the other hand 42 patients had middle level anxiety and the remaining 6 had high anxiety level, whereas the controls, 39 of 43 had middle and 4 had high anxiety level, however, the differences in both the presence or levels of anxiety did not reach the statistical significance, (P>0.05). From other point of view, combination of anxiety and depression was assessed, and revealed that 55 RA patients had depression and/or anxiety compared to 44 controls, with no statistically significant differences between groups, (P>0.05). However, further assessment and comparisons were made between RA and controls in mean total PHQ9 score and mean total anxiety score , where both scores compared as continues variable, this analysis revealed that RA patients had significantly higher PHQ9 score (mean score: 8.08 ± 3.57) than controls (mean score: 6.56 ± 3.60), (P = 0.003), also RA patients had significantly higher mean total anxiety score (mean: 35.88 ± 6.64) than controls (mean: 33.62 ± 5.98), (P = 0.012) (Table 7, Figures 2 and 3).

Moreover, when the participants asked about the difficulty to work, take care of things at home, or get along with other peop le due to the problems they did check in the PHQ-9, 71 RA patients and 68 controls reported no difficulty at all, 26 RA patients and 32 controls had somewhat difficult and only 3 RA patients said that it was very difficult, however, the difference between RA and control groups was statistically insignificant, (P>0.05) (Table 8).

A bivariate correlation analysis was performed to assess these correlations using both Pearson's and Spearman's correlation tests, the correlation matrix is shown in Table 9. Three significant correlations had been reported in these analyses; A significant direct (positive) correlation between total PHQ-9 score and disease duration (R = 0.202, P = 0.044) (Figure 4). A significant direct (positive) correlation between total PHQ-9 score and duration of biological therapy (R = 0.210, P = 0.042) (Figure 5). A significant direct (positive) correlation between total PHQ-9 score and CDAI level (R = 0.230, P = 0.021) (Figure 6).

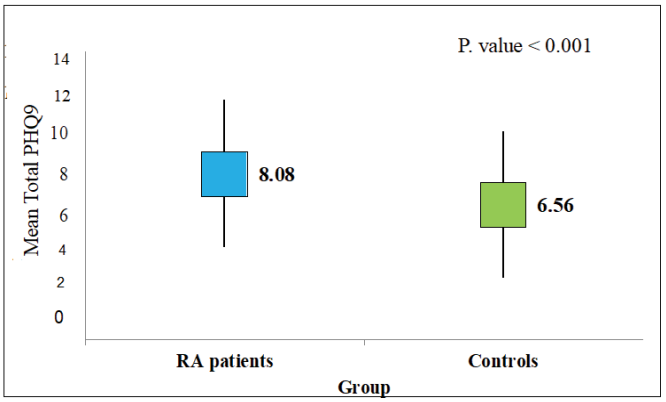

Figure 2: Graphical comparison between RA patients and controls in mean total PHQ9 score.

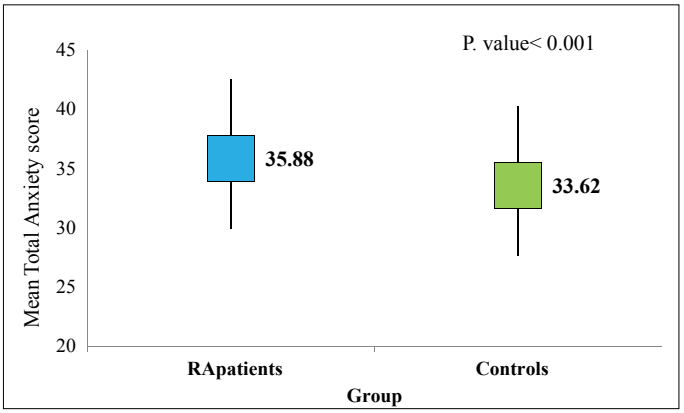

Figure 3: Graphical comparison between RA patients and controls in mean total anxiety score.

Table 8: Difficulty to work, take care of things at home, or get along with other people due to the problems they did check in the PHQ-9, of RA patients and controls.

	Group			
	RA patients (n=100)		Control (n=100)	
Difficulty of problem	No.	%	No.	%
Not difficult at all	71	71.0%	68	68.0%
Some what difficult	26	26.0%	32	32.0%
Very difficult	3	3.0%	0	0.0%
P = 0.158				

Table 9: Correlation matrix of depression and anxiety with other variables of RA patients.

	Total PHQ9		Anxiety score	
	R*	P value	R	P value
Age year	-0.039	0.703	0.035	0.730
Gender	0.140	0.164	0.104	0.305
Marital status	-0.162	0.107	-0.126	0.212
Education	-0.102	0.311	-0.075	0.460
DM	-0.113	0.262	-0.008	0.940
HT	0.022	0.825	-0.147	0.146
Other	0.061	0.546	-0.186	0.064
BMI(kg/m²)	0.141	0.161	0.190	0.058
Smoking Status	0.137	0.174	0.090	0.373
Amount pack	-0.147	0.549	-0.383	0.106
Disease duration	0.202	0.044	0.206	0.040
Duration of biological therapy(year)	0.210	0.042	0.270	0.007
CDAI	0.230	0.021	0.239	0.017
ESR	0.158	0.118	-0.104	0.303
RF	-0.060	0.553	-0.028	0.784
ACPA	0.080	0.427	0.115	0.255
Steroid	-0.151	0.135	-0.140	0.166
DMARDS	-0.087	0.389	-0.165	0.100
MTX	-0.025	0.802	-0.195	0.051
Leflunomide	0.084	0.408	-0.013	0.895
HCQ	0.002	0.982	-0.093	0.357
Azathioprine	-0.178	0.077	0.165	0.100
Sufasalazine	0.076	0.453	0.089	0.376

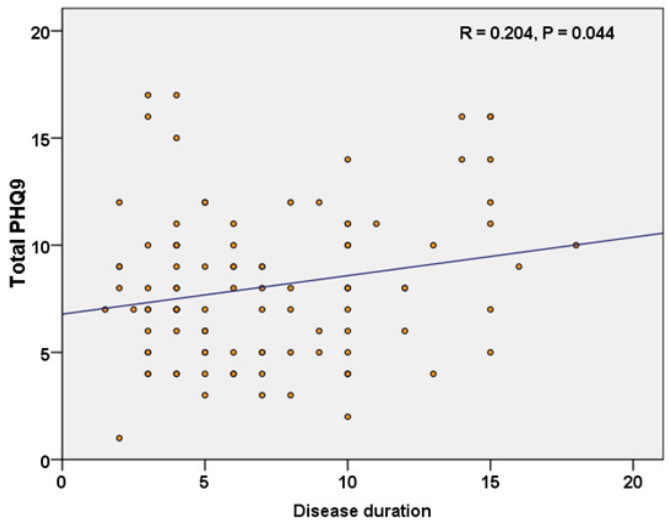

Figure 4: Regression curve estimation of the correlation between total PHQ9 score and disease duration.

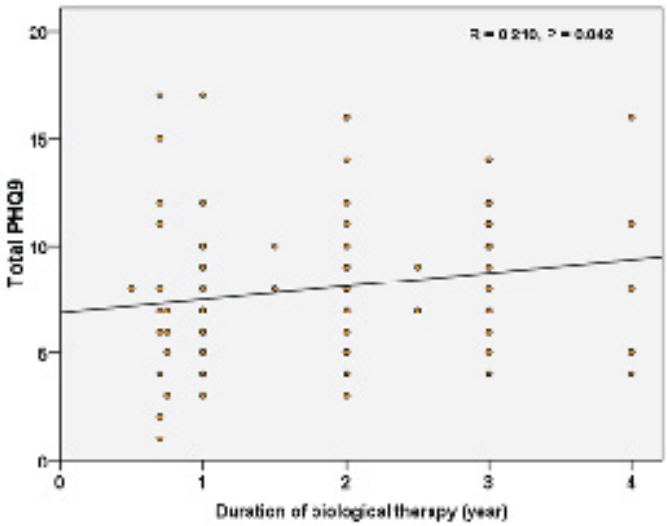

Figure 5: Regression curve estimation of the correlation between total PHQ9 score and duration of biological therapy.

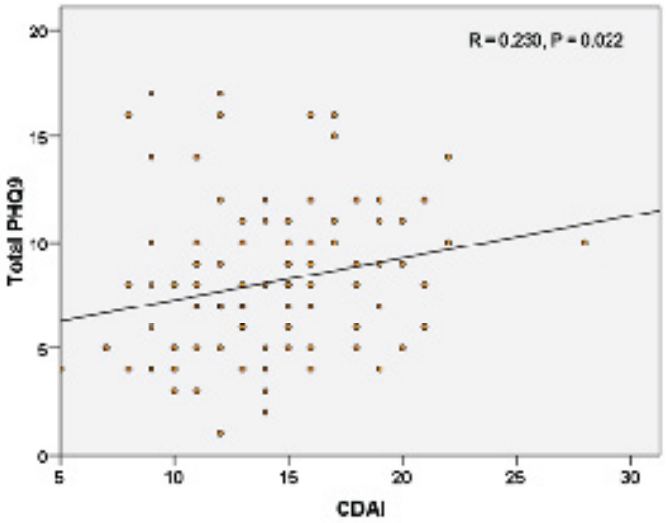

Figure 6: Regression curve estimation of the correlation between total PHQ9 score and CDAI.

Similarly, the anxiety score was directly (positively) correlated with disease duration (R = 0.206, P = 0.040) (Figure 7). Similarly, the anxiety score was directly (positively) correlated with disease duration (R = 0.206, P = 0.040) (Figure 7), duration of biological therapy (R = 0.270, P = 0.007) (Figure 8). And directly (positively) correlated with CDAI levels (R = 0.239, P = 0.017) (Figure 9).

Neither the total PHQ-9 score nor the total anxiety score had significant correlation with the demographic variables , history of medication used, ESR, level, RF positivity, ACPA positivity, DM, Hypertension, or other comorbidities, (P>0.05).

Figure 10 shows the distribution of biological treatment used for RA patients; 42 (42%) used infliximab, 39 (39%) Etanercept and 19 (19%) Adalimumab.

As it shown in table 10, no significant association between depression and type of biological treatment (P>0.05); where depression was reported in 6 patients (14.3%) out of 42 infliximab users, 7/39

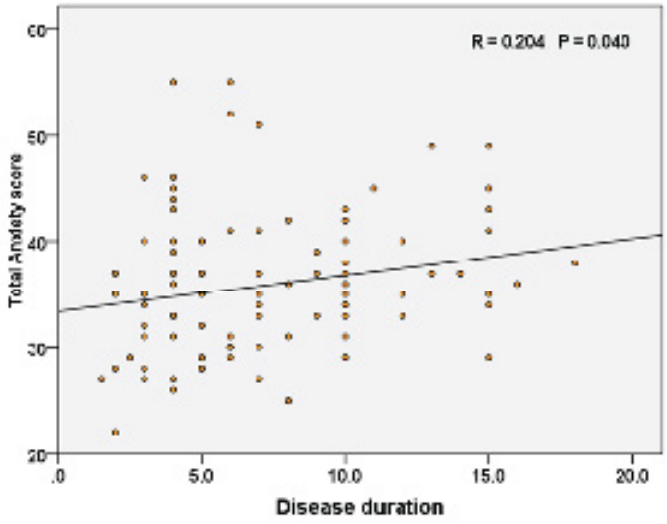

Figure 7: Regression curve estimation of the correlation between total anxiety score and disease duration.

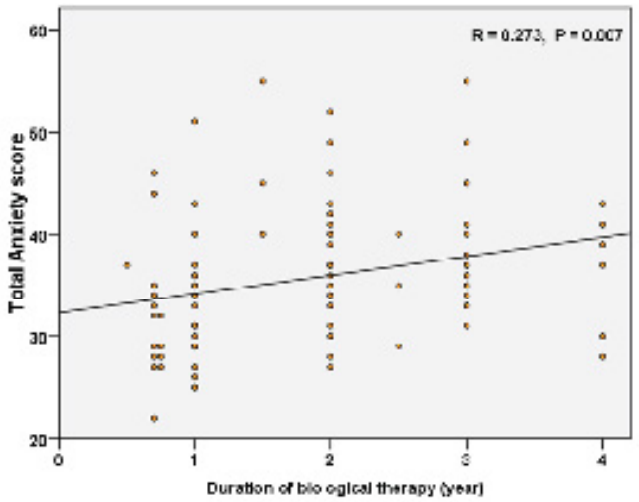

Figure 8: Regression curve estimation of the correlation between total anxiety score and duration of biological therapy.

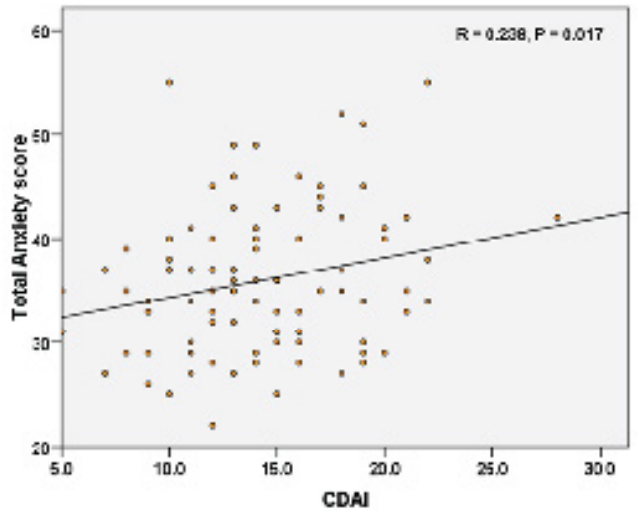

Figure 9: Regression curve estimation of the correlation between total anxiety score and CDAI.

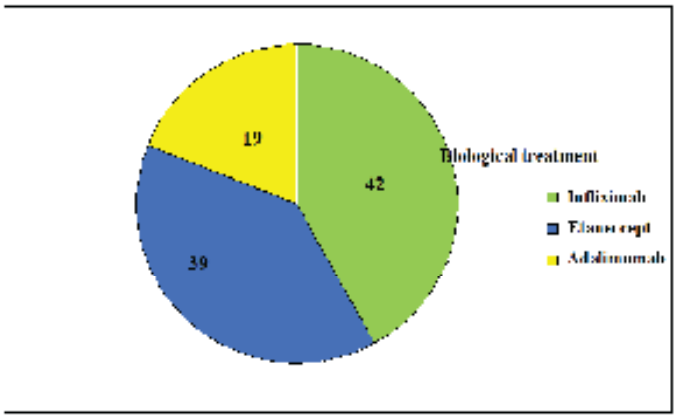

Figure 10: Distribution of biological treatment in RA patients.

Table 10: Relationship between type of biological treatment and depression among RA patients.

Subgroup	Depression				Total
	Positive (n=16)		Negative (n=84)		
	No.	%	No.	%	
Infliximab user (n= 42)	6	14.3	36	85.7	42
Etanercept user (n= 39)	7	17.9	32	82.1	39
Adalimumab user (n= 19)	3	15.8	16	84.2	19

Table 11: Comparison of mean total PHQ across the type of biological treatment.

	Total PHQ	
Subgroup	Mean	SD
Infliximab user (n= 42)	8.357	3.41
Etanercept user (n= 39)	7.718	4.03
Adalimumab user (n= 19)	8.211	2.97

(17.9%) of Etanercept users and 3/19 (15.8%) of Adalimumab users.

Furthermore when the mean total PHQ score of RA patients compared across the type of biological treatment, using ANOVA test, no significant differences had been found among the mean total PHQ scores of those used infliximab, Etanercept or Adalimumab, (P>0.05) (Table 11).

Discussion

Rheumatoid Arthritis chronic inflammatory disease follows a progressive debilitating course which affects the quality of life, Chronic painful state of disease and undefined period of treatment severely impair psychological well-being [10]. In this study, a 100 RA patients treated by biological drugs (ANTI-TNF) were evaluated for anxiety and depression and their relationship with disease activity. The current study showed that depression and anxiety in RA patient treated with biological drugs were higher (not significantly) differ from control. Possible explanation of depression and anxiety in RA may be due to systemic inflammation of disease contributes to the high prevalence of depressive symptoms in patients with RA as depressed patients have activated inflammatory pathways, including increased expression of chemokines, adhesion molecules and cytokines and proinflammatory TNF- α or there is some genetic loci associated with psychiatric disorders have pleiotropic effects and may be associated with depression or may be shared environmental factors such as chronic illness , undefined period of treatment severely impair psychological well-being [10-12] .

Psychiatric comorbidity is associated with adverse outcomes in RA, were associated with higher levels of pain and disability, increased

health service utilization and are less likely to be adherent with their medications [13]. About 40% reduced likelihood of clinical remission at 1 year [14]. The results were consistent to Turkish study by Uguz F, et al. (2009) [15] that found anti-TNF-alpha drugs may reduce anxiety and depressive symptoms by affecting elevated TNF- a-induced changes in neurotransmitter release or functions, were found inflammatory cytokines and acute-phase reactants are increased in depressive symptoms in patients without RA [12]. Also the result agree with previous study made by Abbottet, that showed the treatment with TNF-α improve depression and anxiety, it fails to indicate whether the mechanisms of improving depression are directly mediated by a reduction in TNF-α or whether the benefits to depression are secondary to reductions in pain and disability associated with improvement in chronic inflammatory condition.

In this study ,when comparison done between RA and control in mean total PHQ9 and mean total anxiety score showed that its higher in RA than control as this consistent to Covic T, et al. (2012) [16] that revealed higher rate of depression and anxiety are there is close association between depression and pain. The clinical disease related variables and medication of RA patients are shown in table 9 were showing positive correlation of anxiety and depression with disease duration, disease activity, duration of biological treatment. While other parameters as mean ESR, other DMARD and steroid using showing insignificant association (P value >0.05).

These results are consistent with previous studies as conducted by 17. Kwiatkowska B, et al. (2018) [17], Margaretten M, et al. (2009) [18], which showed that long-term disability and joint damage associated with arthritis leads to depression in patients with RA. Soósová MS, et al. (2017) [19] found that anxiety and depression are proportionally worse with longer duration of RA. Matcham F, et al. (2016) [20] had shown an increase in anxiety and depression with increased levels of tenderness and poor patient global assessment. Hider SL, et al. (2019) [21] showed that depression is associated with poorer responses to anti-TNF drug, as this increases disease activity over time which lead to slower achievement of remission. Rathbun AM, et al. (2012) [22] had showed that depression impacts RA patients in several ways. Depression may worsen pain and disease activity; though it is unclear whether this is via a response shift created by repetitive negative thinking, immunologically mediated mechanisms that affect inflammation or a combination of psychological, behavioral and biological factors that impact the sensation of pain and decreased patient response to pharmacological treatment.

All demographic data showed insignificant association (p value >0.05), one explanation most patients enrolled in the study were females and our sample was dominant for married and uneducated ,also this could be due to sample size, stress of our environment. Also the type of Anti-Tumor Necrosis Factor used in treatment of RA patients has shown no specific correlation with depression were all them had implicated in reduction of depressive and anxiety symptom as shown by Uguz F, et al. (2009) [15].

Conclusion

Depression and anxiety has been lower in RA patients treated with anti TNF drugs. The coexistence of depression and or anxiety with RA negatively impact the scores of disease activity in RA patients. Depression and anxiety in RA were associated with poor response to anti TNF drugs. Depression and anxiety should be evaluated in RA patients. Recognition and appropriate management of depression and anxiety can improve anti TNF drugs therapy effectiveness. Future studies that include larger numbers of patients and use of biological parameter is recommended to validate the finding of this study.

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