World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
Volume-16, November 2022
ISSN: 2749-3644

PREVALENCE OF DEPRESSION IN A SAMPLE OF IRAQI PATIENTS WITH RHEUMATOID ARTHRITIS

Dr. Ahmed Salahuddin M. Rhida[1],
Dr. Rana Jabar Mahdi[2]
Alfurat general hospital, Baghdad-Alkarkh health directorate, Ministry of health, Iraq
1Email: salaha798@yahoo.com
2Email: rjbar6067@gmail.com

Article history:

Received: September 13th 2022
Accepted: October 14th 2022
Published: November 20th 2022

Abstract:

Background: Rheumatoid arthritis (RA) is a common chronic systemic autoimmune inflammatory disease that affects all ethnic groups throughout the world. It leads to chronic articular, extra-articular manifestations and disability. Depression is a common sequel of RA and it is a mental illness characterized by a profound and persistent feeling of sadness or despair and\or loss of interest. Depression is important contributor to poor health outcome in RA patients.

Objectives: To assess the current prevalence of depression and its severity in Patients of RA. To analyze the effect of sociodemographic factors and variables related to RA disease on development of depression.

Patients and Methods: A randomly selected samples of diagnosed RA patients attending rheumatology unit in Baghdad Teaching Hospital (total=100, female=87, male=13)diagnosed by American Rheumatism Association 1987 revised criteria for rheumatoid arthritis classification and The 2010 American College of Rheumatology/European League Against Rheumatism classification criteria for rheumatoid arthritis , the patients were subjected to a questionnaire for sociodemographic data and variables related to RA disease and diagnosing the presence of depression by the semi-structure Arabic version questionnaire of the International Statistical Classification of Diseases and Related Health Problems 10th version(ICD 10)criteria for the diagnosis of depression . Data was collected in period between14thof October 2012 to 24th of March 2013. Data was statistically analyzed by (Statistical Package for Social Sciences) in association with Excel version 5.

Results: Current prevalence of depression in RA patients was found to be 55% (male 30%, female 58.6%). Statistically significant difference was found between patients on steroid and that not on steroid, the low socioeconomic status showed obvious effect in development of depression, regarding sex study showed obvious increase in depression among females, by analysis the marital status groups (being widow or divorced may be a risk factor for developing depression), the study showed low prevalence of ideas or acts of self-harm or suicide among RA patients with depression.

Conclusions: The prevalence of depression in this study, amounting to 55% was considered higher than the ratio found in other studies in the world, it was found that having depression in rheumatoid arthritis more in patients on long term steroid, females, low socioeconomic status and patients with partner loss, while use of DMARDS and biologic agents, disease duration and smoking habit had no significant effect on development of depression among RA patients.

Keywords: Rheumatoid arthritis, Depression

World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
Volume-16, November 2022
ISSN: 2749-3644

INTRODUCTION

Rheumatoid arthritis is a systemic inflammatory disease of unknown cause that mainly affects the joints, its main feature consists of chronic inflammation of the synovium, which may in time lead to massive articular destruction and accentuated disability, there may be involvement of multiple organs and extra-articular systems(1).

Epidemiology, Women are affected by rheumatoid arthritis approximately 3 times more often than men (2). The annual incidence of rheumatoid arthritis is approximately 3 cases per 10,000 population and the prevalence of rheumatoid arthritis in Iraq is 1 % in those aged 16 years or more comparable to that recorded in northern Europe(3).

Etiology: A) Genetic factors: First-degree relatives of rheumatoid arthritis are 1.5 folds higher than general population (4).

B) Non-genetic factors: Sex: females are 2-3 times higher than males (4).

Other factors like smoking ,Bacteria and viruses are considered as initiating factors for RA (4,5).

Pathophysiology and pathogenesis: The rheumatoid synovium is characterized by the presence of a number of secreted cytokines and chemokine of activated lymphocytes, macrophages, and fibroblasts ,which account for many of the pathologic and clinical manifestations of RA(6).

Clinical features: The clinical presentation of rheumatoid arthritis varies, but an insidious onset of pain and symmetric swelling of synovial-lined joints including, metacarpophalangeal, proximal interphalangeal and metatarsophalangeal joints, as well as in the wrists and knee, morning stiffness in and around the joints, lasting at least 1 hour before maximal improvement is a typical sign of rheumatoid arthritis, also fatigue, fever, weight loss, and malaise are frequent clinical symptoms (7).

Extra-articular manifestations occur in seropositive patients and include rheumatoid nodules, Sjögren's syndrome, interstitial lung disease, and vasculitis(8).

Diagnosis: There is no single clinical, radiological, serological test which enables the diagnosis of rheumatoid arthritis to be made with certain; the diagnosis depends upon the aggregation of characteristic symptoms, signs, laboratory data, and radiological finding (9).

American Rheumatism Association revised criteria for rheumatoid arthritis classification in 1987 (10). The 2010 American College of Rheumatology/European League Against Rheumatism classification criteria for rheumatoid arthritis (11).Management (1)Non pharmacological therapies Rheumatoid arthritis patients should have easy access to physiotherapy, occupational therapy, psychological services and there should be regular review, particularly with physiotherapy and occupational therapy(12).

(2)Medication-based therapies comprise several classes including:

(a)Nonsteroidal anti-inflammatory drugs:for example ibuprofen, diclofenac, naproxen (13).

(b) Corticosteroids:

Most of the desired clinical effects of corticosteroids treatment in rheumatic patients are mediated by transrepression; these include the reduction of clinical signs and symptoms of inflammation and the retardation of the radiological progression (14).

The somatic adverse effects of corticosteroid therapy like cardiovascular, dermatologic, endocrine, gastrointestinal and others, has been extensively researched and widely described, while the neuropsychiatric adverse effects have received less attention, the most commonly reported corticosteroid-induced psychiatric disturbances are affective , including mania, depression, or mixed states ,but most common adverse effects of short-term corticosteroid therapy are euphoria and hypomania, conversely, long-term therapy tends to induce depressive symptoms(15).

(c) Disease-modifying antirheumatic drugs

Include: Hydroxychloroquine , leflunomide, methotrexate, sulfasalazine, azathioprine (16).

(d) Biological therapies:

Adalimumab, Certolizumab Pegol, Etanercept, Golimumab, Tocilizumab (17).

(3) Surgical therapy: necessary to relieve pain or diminish the functional impairment secondary to alterations in joint function (18).

Depression is a part of normal experience to feel unhappy at time of adversity, while depressive disorder (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 least 2 weeks (19,20).

Clinical features:

absence of a positive affect, Low mood with a range of associated emotional and cognitive symptoms, behavioral and physical symptoms typically include tearfulness, irritability, social withdrawal, an exacerbation of pre-existing pain, and pain secondary to increased muscle tension, a lack of libido, fatigue and diminished activity, although agitation is common and marked anxiety frequent, there is reduced sleep and lowered appetite (20,21).

Diagnosis:

There are 2 diagnostic criteria for the diagnosis of depression (22,23): Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-4) and International Statistical Classification of Diseases and Related Health Problems 10th version (ICD10), depressive episode according to ICD-10 criteria, which used by WHO.

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ISSN: 2749-3644

Association of Depression and Rheumatoid Arthritis Rheumatoid arthritis can increase the frequency of depression, depression manifested by fatigue, sleep disturbance and decrease level of compliance with medications which actually worsen rheumatoid arthritis symptoms (24). Corticosteroid is one of the medications used in RA which has many side effects, Psychiatric adverse effects during therapy are common. Two large meta-analyses found that severe reaction so occurred in nearly 6% of patients, and mild to moderate reactions occurred in about 28%, although disturbances of mood, cognition, sleep, and behavior as well as frank delirium or even psychosis are possible, the most common adverse effects of short-term corticosteroid therapy are euphoria and hypomania, conversely, long-term therapy tends to induce depressive symptoms (25).

AIM OF THE STUDY:

1. To find out the prevalence of depression and its severity among patients with rheumatoid arthritis.
2. To analyze the effect of socio-demographic and rheumatoid arthritis related variables in the development of depression in those patients.

PATIENTS AND METHODS:

Patients

A cross sectional study consisted of 100 patients (13 males, 87 females with age range 20-70 years) ,the study subjects were chosen from the patients who attended the outpatient unit of Rheumatology of Baghdad Teaching Hospital in Medical City between14thof October 2012 to 24th of March 2013, all the patients met the revised criteria of American College of Rheumatology (ACR) for RA in 1987 and The 2010 American College of Rheumatology/European League Against Rheumatism classification criteria for Rheumatoid arthritis with no previous history of any psychological illnesses or psychiatric consultations prior to getting the RA disease. The patients were chosen randomly and fit to the inclusion criteria of the study.

METHODS

The instrument includes:

1.The first part includes : the sociodemographic data of the patients regarding their age, sex ,marital status ,occupation ,income, educational level, socioeconomic status ,smoking habit and variables related to RA patients including duration of disease, rheumatoid factor, types of medications (dose, duration), past medical history and past psychological history . 2. The second part includes: Patients were attended to psychiatry outpatient unit for diagnosing the presence of depression by the semi structure arabic version questionnaire of the ICD 10 criteria. Each respondent was interviewed alone, in an isolated room with in 20 to 30 minutes, under the psychiatrist supervision. 3. The third part includes: The patient who diagnosed as having depression, was given Beck Depression Inventory (BDI) Arabic version in a paper. The patient would read the inventory by his own and respond by indicating the statement which best describes how he/she has felt in general over the past week. For those how can't administer the test by their own either because they were illiterate or that they had a poor vision , the interviewer would read the inventory on his paper allowing the patient to respond by indicating the statement which best describes how he/she has felt in general over the past week . The responses of the patients to Beck Depression Inventory were analyzed to find how it can verify symptom .

Ethical Issues:

The permission was taken from my psycatry supervisor in the psycatry outpatient unit in Baghdad Teaching Hospital to perform this study, and verbal consent was taken from each respondent before establishing the individual interview.

Inclusion criteria:

Patients of both sexes, ranging from 20-70 years old, with confirmed diagnosis of rheumatoid arthritis by the revised 1987 American Rheumatism Association criteria(10) and The 2010 American College of Rheumatology/European League Against Rheumatism classification criteria for Rheumatoid arthritis (18).

Exclusion criteria:

Any participants having history of depression prior to having RA disease, or having organic brain disorder.

Statistical analysis:

Data were translated into a computerized database structure. The database was examined for errors using range and logical data cleaning methods, and inconsistencies were remedied. An expert statistical advice was sought for. Statistical analyses were done using SPSS version 20 computer software (Statistical Package for Social Sciences) in association with Excel version 5. Frequency distribution for selected variables was done first. Associations between 2 categorical variables were explored by crosstabulation. The statistical significance of such associations was assessed by Chi-square (x2) test of homogeneity or Fisher's exact test (when the condition for a valid chi-square test are not met). To measure the strength of association between association between a dichotomous independent variable (a specific group compared to reference group) and a dichotomous outcome variable (like having depression) the prevalence ratio (PR) which is similar in calculation to RR (relative risk) was used. PR equals the ratio between prevalence of outcome (depression) among those with risk factor divided by prevalence rate among those negative for the risk factor. The relative

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Available Online at: https://www.scholarexpress.net
Volume-16, November 2022
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risk is the real measure of association between exposure to a certain factor and having the disease or outcome, but it needs a cohort study, in which the exposure status is determined first and the study subjects are followed for a long period of time to assess the development of the disease of interest. The present study is a crosssectional study, in which the calculated PR can provide an estimate for the real measure of risk (RR) which can be calculated in cohort studies only. The logarithm method was used in calculation of confidence intervals for PR (26).

		DEPRSSION	
		+	_
	+	A	B
Presence of specific risk factor	_	C	D

$$PR = \frac{\frac{A}{A+B}}{\frac{C}{C+D}}$$

The 95% confidence interval is a statistical procedure to anticipate or predict the expected range of possible values of the calculated sample estimate of any statistic in the reference population with 95% confidence.
Reference category: In any estimate of risk the calculated index measures the risk for one category in comparison to a reference category, which always has a risk of one (neutral).
A multiple logistic regression model with selected factors as independent variables and having depression as the dependent variable was used. The model assess the risk of having depression for each explanatory variable after adjusting for the effect of other confounders included in the model. The model provides the following parameters: P value for the model: In order to generalize the results obtained, the model should be statistically significant. Predictive power of the model: The overall predictive power is expressed as percentage of study subjects being classified correctly based on calculated parameters. Partial OR (odds ratio): the risk of having the outcome in the presence of a specific risk factor. Each OR is adjusted for the effect of other explanatory variables included in the model, to represent a net effect of each factor on the Depression risk of having the outcome. The OR for different explanatory variables in a subject are additive, in other words the risk of having the outcome in a specific subject is the sum of the OR for the whole set of explanatory variables, P value for OR: reflects the statistical significance of the calculated OR(54).

RESULTS:

A total sample of 100 Iraqi RA patients consist of (87.0% females,13.0%males)and the age of them is between 20-70 years with disease duration ranging from 6 months to 25 years,(42.0%) are testing positive for rheumatoid factor ,the sample is also assessed for smoking habit and marital status in which married are(78.0%) as shown in table 1.

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Volume-16, November 2022
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Table 1: Frequency distribution of the study sample by selected variables.

		Number	%
1.	Age group (years)		
	< 40	34	34.0
	40-50	29	29.0
	50+	37	37.0
	Total	100	100.0
2.	Duration of RA categories (years)		
	<5	38	38.0
	5-9	26	26.0
	10+	36	36.0
	Total	100	100.0
3.	Smoking habit		
	Never smoked	86	86.0
	Ex-smoker	8	8.0
	Current smoker	6	6.0
	Total	100	100.0
4.	RF		
	Negative	58	58.0
	Positive	42	42.0
	Total	100	100.0
5.	Marital status		
	Single	14	14.0
	Married	78	78.0
	Widow	5	5.0
	Divorced	3	3.0
	Total	100	100.0

According to ICD 10 criteria for the diagnosis of depression, the prevalence of depression in the study sample is 55.0% (male 30.0%, female 58.6%)and 95% confidence interval for prevalence rate = (45.2 –64.8)% as shown in (Table 2).

Table 2: Frequency distribution of the study sample by variables used in calculation SES (socio-economic status).

	Number	%
Diagnosis of depression (ICD10)		
Negative	45	45.0
Positive	55	55.0
Total	100	100.0

Regarding the types of treatments that RA patients receiving and their percent including: Methotrexate 74(74.0%), other types of DMARDS 29(29.0%), biologic agents 27(27.0%) and 72(72.0%) for steroid use as shown in (Table 3).

Table 3: Prevalence rate of depression in a sample of 100 cases with RA.

	Number	%
MTX use	74	74.0
Other DMRAD use	29	29.0
Biologic agents	27	27.0
Steroid use	72	72.0
Total	100	100.0

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Available Online at: https://www.scholarexpress.net
Volume-16, November 2022
ISSN: 2749-3644

In our sample of RA patients using variable treatments shows the rate of depression among subjects using steroid which is (65.3%) higher than those who do not use steroid (28,6%) and this result is statically significant (p value< 0.001) ,while the remaining treatments used for RA (Methotrexate, other DMRADS and biologic agents) had no important or statistically significant association with the risk of having depression as shown in (Table4).

Table 4: The rate of depression by drugs used for treatment

Total (ICD10)	Diagnosis of depression				
	N	N %	P	PR	95% CI of PR
MTX use					
Negative	26	14	53.8	0.89 [NS]	Ref
Positive	74	41	55.4	1.03	(0.68 - 1.55)
Other DMRAD use					
Negative	71	38	53.5	0.64 [NS]	Ref
Positive	29	17	58.6	1.1	(0.76 - 1.6)
Biologic agents					
Negative	73	42	57.5	0.4 [NS]	Ref
Positive	27	13	48.1	0.84	(0.54 - 1.3)
Steroid use					
Negative	28	8	28.6	<0.001	Ref
Positive	72	47	65.3	2.28	(1.24 - 4.19)

By studying multiple variables in our sample show no statically significant effect on developing depression including age, gender, SES, duration of RA and use of selected treatments of RA apart from significant effect of long term steroid(p value0.001)(OR 24.2) as shown in (Table 5)

Table 5: Multiple logistic regression models with the risk of having depression as the dependent (outcome) variable and age, gender, SES, duration of RA and use of selected treatments as explanatory (independent) variables.

	OR	P
Age group (years)		0.7[NS]
(40-50 years old) compared to <40 years		1.74
0.4[NS]		
(50+ years old) compared to <40 years		1.32
0.66[NS]		
Male gender compared to female		0.23
0.06[NS]		
SES (socio-economic status)		0.14[NS]
Intermediate SES compared to low SES		1.19
0.76[NS]		
High SES compared to low SES		0.37
0.12[NS]		
Use of DMARD		1.16
0.82[NS]		
Use of Biologic agents		0.66

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Available Online at: https://www.scholarexpress.net
Volume-16, November 2022
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0.44[NS]		
MTX duration of use categories		
0.64[NS]		
Short duration of MTX use (<2 years) compared to non-users		1.70
0.49[NS]		
Average duration of MTX use (2-5 years) compared to non-users		0.81
0.79[NS]		
Long duration of MTX use (6+ years) compared to non-users		
0.67 0.65[NS]		
Steroid duration of use		
0.004		
Short duration of steroid use (<2 years) compared to non-users		
3.5 0.07[NS]		
Average duration of steroid use (2-5 years) compared to non-users		5.3
0.007		
Long duration of steroid use (6+ years) compared to non-users		24.2
0.001		
Duration of RA		0.99
0.97[NS]		

To study the net and independent effect of a set of explanatory variables on the risk of having depression in a sample of cases with RA a multiple logistic regression model was used. Age, gender, SES, duration of RA and use of selected treatments were tested for their explanatory power. The model was statistically significant with an overall classification accuracy for the outcome (having depression) of 76%. Only steroid use showed a statistically significant positive association with the risk of having depression after adjusting (controlling) for the possible confounding effect of other explanatory variables included in the model.

A long duration of steroid use (6+ years) increases the risk of having depression by 24.2 times compared to non-users of steroids. An average duration of steroid use (2-5 years) increases the risk of having depression by 5.3 times compared to non-users of steroids. A higher age marginally increases the risk of having depression, but the calculated OR (odds ratio) was not significant statistically. Male gender obviously reduce the risk of having depression by more than 4 times (OR = 0.23) compared to females after adjusting (controlling) for the possible confounding effect of other explanatory variables included in the model. The calculated OR for gender effect failed, however to reach the level of statistical significance. A high SES obviously reduce the risk of having depression by an almost 3 times (OR = 0.37) compared to those with low SES after adjusting (controlling) for the possible confounding effect of other explanatory variables included in the model. The calculated OR for SES also failed to reach the level of statistical significance. Duration of the disease had no obvious or statistically significant association with the risk of having depression. Apart from steroids the remaining treatments used for RA (DMRADS, biologic agents and MTX) had no important or statistically significant association with the risk of having depression.

DISCUSSION:

Rheumatoid arthritis can increases the frequency of depression, and negative emotions have been shown to influence adaptations among patients with RA (27). Our study showed that the prevalence of depression among RA patients found to be 55% (male 30.8%, female 58.6%) and this result was higher than two other studies were done in USA and Turkey showing its prevalence as (30.0%) and (41.0%) respectively (28,29), this may be due to difficult situation in Iraq in regard to security, political, social, and economical aspects. In our study regarding the effect of medications of RA patients, it showed that statistically significant prevalence among RA patients on long duration of steroid use (6+ years) increases the risk of having depression by 24.2 times compared to non-users of steroids and average duration of steroid use (2-5 years) increases the risk of having depression by 5.3 times compared to non-users of steroids which were in agreement with Bolanos et al(30) and Lewis and Smith(31), they found that long-term steroid therapy was more frequently associated with depressive symptoms.

Concerning the effect of gender factor had shown obvious difference between males and females, which was found to be more in females(58.6%) than

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Available Online at: https://www.scholarexpress.net
Volume-16, November 2022
ISSN: 2749-3644

males(30.6%), comparable to previous study done by Dowdy et al (32) ,which showed that female gender was a risk factor , this may be attributed to the fact that the majority of the sample were females (87.0%)and by the fact that women in our society are exposed to much stress than men due to feeling of being neglected by their families and being a burden on the society.

Regarding the severity of depression among depressed patients with rheumatoid arthritis according to Beck's Depression Inventory, it showed that majority of them were having moderate severity 32(32.0%),m18(18.0%) severe depression and only 5(5.0%) mild, these results showed that the larger group of patients in the moderate category and there was no related researches about this motif.

Analysis of the effect of socioeconomic status had shown the distribution of depression in rheumatoid arthritis patients according to socioeconomic status, and it showed that a significant difference between high and low socioeconomic status in which depression was more prevalent in low socioeconomic status (65.6%), this result may be due to inability of such patients to provide medications and equipment's necessary to control the disease.

About the effect of age which showed the distribution of depression among rheumatoid arthritis patients according to age groups and it found no statistically significant difference among them similar to Ang, et al.study which showed no significant difference among age groups (33). Analysis of the effect of marital status showed that the prevalence of depression was more in the widow or divorced patients (100%) when compared to the married or single group (51.3%) and (50.0%) respectively, this result was in agreement with other studies which found that the absence of a marital partner may hasten the onset of depression among vulnerable individuals (60,61),including RA patients (36).

Regarding the effect of depression symptoms in patients with rheumatoid arthritis plus depression, showed low prevalence of ideas or acts of selfharm or suicide among RA patients with depression, this result may be due to the religious principles that predominate in the Iraqi society which forbidden suicide.

CONCLUSIONS

- In our study the prevalence of depression in RA patients is 55.0% (male 30.8%, female 58.6%).
- Long term uses of steroids in the treatment of RA, female sex, low socioeconomic status and the loss of the partner are risk factors for developing depression in RA patients.
- The Relationship between the development of depression in RA patients and the effect of age group, duration of illness, rheumatoid factor and smoking habit reveals no significant differences.

RECOMMENDATIONS

- Performing more studies about the prevalence and the risk factors for mental illnesses in rheumatic patients.
- Steroid should be used wisely in the treatment of RA because its long term use may cause depression in RA patient.
- Training of rheumatologist to do initial psychiatric interview, revealing mental illnesses, and advised to send RA patients for psychiatrist when necessary.

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