

Original Article

The Prevalence of Depression in People with Rheumatoid Arthritis

Yousif Mufaz Myhydeen

Primary Health Corporation, Consultant Doctor in Family Medicine, Qatar.

Received: 03 January 2023

Revised: 06 February 2023

Accepted: 17 February 2023

Published: 28 February 2023

Abstract - Inflammation of the joints and other body systems are hallmarks of rheumatoid arthritis (R.A.), a chronic autoimmune inflammatory disease. It has been suggested in the recent literature that R.A. may be linked to depression. In R.A., depression is more common than in the general population. It has been associated with more pain and fatigue, worse quality of life in terms of health, more significant physical disability, and higher medical costs. Patients with Rheumatoid Arthritis who are depressed have worse long-term outcomes, including tremendous pain and mortality. So, therapies for depression that attempt to boost patients' perceptions of their health and well-being might be pretty effective. The purpose of this study is to use the Patient Health Questionnaire-9 (PHQ-9) to determine the prevalence of depression among patients with a confirmed diagnosis of rheumatoid arthritis, as well as to examine its relationship with disease activity and to compare it to that seen in the general population. A case-control study with 50 consecutive patients diagnosed with R.A. according to the ACR/EULAR diagnostic criteria for Rheumatoid Arthritis and 50 healthy controls. Questionnaires and in-depth interviews were used to compile the data. Subjects disclosed their ages, sexes, socioeconomic statuses, illness diagnoses, disease durations, quality of life, and medicines Using the DSM-IV criteria; depression was measured using the PHQ-9. The clinical Disease Activity Index was used to evaluate disease prevalence (CDAI). Patients had a mean age of 47.3 12.8 years old, while controls were 38.1 14.2 years old. For every 50 patients, 39 were diagnosed with depression, whereas only 22 of the controls did so. Patients with Rheumatoid Arthritis had a significantly higher rate of major depression than the control group. Patients with Rheumatoid Arthritis showed a strong correlation between depression severity and disease activity. Rheumatoid arthritis patients were shown to have a higher-than-average rate of depression, which was linked to worse disease outcomes. These findings indicate the need for depression screening and treatment as part of effective R.A. therapy.

Keywords - Prevalence, Depression, People, Rheumatoid, Arthritis.

1. Introduction

Rheumatoid arthritis (R.A.) is characterized by inflammation throughout the body and commonly manifests as polyarticular slight joint arthritis in the hands and feet. This disorder may cause cartilage and bone deterioration, joint abnormalities, persistent functional impairment, and disability ⁽¹⁾. Although rheumatoid arthritis is typically considered a joint disease, aberrant systemic immune responses are apparent and may induce numerous extra-articular symptoms such as vasculitis, nodules, and accelerated atherosclerosis ⁽²⁾.

Multiple studies have pointed to depression as a crucial factor in R.A. There is a wide range of causes for low mood in rheumatoid patients. The cause of mental comorbidity is unknown. However, it may be connected to the immune-inflammatory state or a sign of persistent sickness and impairment ⁽³⁾. Long-term discomfort ⁽⁴⁾, the presence of somatic symptoms ^(5,6), the inability to perform daily tasks ⁽⁷⁾, and the course of the illness ⁽⁸⁾ may all play a role in the onset of depression. ⁽⁵⁾

Approximately 0.5-1 percent of the global adult population has rheumatoid arthritis. The frequency of R.A. has stayed the same, however, since people with R.A. live longer, suggesting that the total incidence of R.A. has declined in recent decades. Rheumatoid arthritis has a different global and national incidence and prevalence across different ethnic groups. Rheumatoid arthritis has a female-to-male prevalence ratio of 2-3:1, similar to other autoimmune disorders ⁽⁸⁾. The late childbearing years are a typical time for R.A. to manifest in women, whereas the sixth to eighth decades are more common for R.A. to manifest in males. ⁽⁹⁾ Patients with rheumatoid arthritis sometimes exhibit symptoms like morning stiffness lasting more than an hour, pain and swelling in the joints of the hands, wrists, and feet, and fatigue ⁽¹²⁾. Patients with Rheumatoid Arthritis may suffer discomfort in the forefeet at the onset of the disease and have trouble utilizing their hands with daily activities. Low-grade fever and weariness are two examples of systemic symptoms that might be present. Swelling (or synovitis), soreness, increased temperature, and restricted range of motion are common findings on examination of the joints ⁽¹³⁾.



Up to 50% of individuals with R.A. may have extra-articular symptoms, and they are associated with a poor prognosis, including higher rates of morbidity and death ⁽¹⁴⁾.

Classification criteria for rheumatoid arthritis were established in 2010 by the American College of Rheumatology and the European League Against Rheumatism. Getting six means to have moderate to severe R.A. (15) appendix 1.

2. Relating Rheumatoid Arthritis to Mood Disorders

Increased job impairment in R.A. patients with comorbid depression has been shown. People with rheumatoid arthritis are more likely to have depression symptoms because they have less time to participate in social and leisure activities. The presence of both illnesses increases the demand placed on the healthcare system by patients needing treatment for their sickness, as shown by an increase in the number of office visits to specialists and primary care doctors, as well as the number of painkillers they require. Negative treatment compliance is linked to depressive symptoms. Rheumatoid arthritis patients suffering from depression are at a higher risk for occupational incapacity, death, and myocardial infarction. Depression raises the risk of ill health and higher healthcare expenditures, hinders everyday functioning, and lowers the quality of life ⁽¹⁶⁾.

This research aims to administer the PHQ-9 questionnaire to persons with a confirmed diagnosis of R.A., analyze the results in connection to disease activity, and compare the results to those of a control group of healthy individuals.

4. Results and Discussion

4.1. Results

Characteristics of the study's representative sample population are shown in Table (1).

Table 1. Characteristics of the Study's Sampled Population

Parameters	Symptoms of Rheumatoid Arthritis [n = 50]	Reduce or eliminate rheumatoid arthritis [n = 50]	P-value*
Mean age (years)	47.3 ± 12.8	38.1 ± 14.2	0.001
Mean duration of R.A. (years)	9.7 ± 6.9	---	---
No. of children	4.4 ± 3.0	3.6 ± 2.9	0.074
Gender	No. (%)	No. (%)	---
Male	6 (12.0)	25 (50.0)	0.001
Female	44 (88.0)	25 (50.0)	
Smokers**	9 (18.0)	20 (40.0)	0.055

* The Chi-square test (d.f. = 1) was used for categorical data, while the Independent T-test of two means was employed for quantitative variables.

** Including x-smokers also.

Table 2: shows how the rheumatoid and control groups compare concerning many socioeconomic indicators. It was statistically determined that there was a big difference

3. Materials and Methods

The Rheumatology Unit of Ibn Sena Teaching Hospital in Mosul conducted a case-control study between October 2020 and March 2021. Ethical permission was granted by the University of Mosul's Medical Department/College of Medicine. All of the study subjects agreed to take part.

The research comprised 50 patients with R.A. and 50 healthy controls, both of whom were classified according to the ACR/EULAR diagnostic criteria for rheumatoid arthritis ⁽¹⁵⁾ Appendix (1).

They should be avoided if they also have known mental health issues and extra connective tissue diseases. We obtained using questionnaires that included demographic and clinical information (age, gender, body mass, socioeconomic class, illness duration, quality of life, and drugs taken ⁽¹⁵⁾ Appendix (2). Based on the DSM-IV criteria ⁽¹⁷⁾ Appendix, depression is measured using the PHQ-9 score ⁽³⁾. Clinical Disease Activity Index (CDAI) ⁽¹⁸⁾ Appendix was used to calculate the level of disease ⁽⁴⁾.

3.1. Analytical Statistics

Input data and analysis were performed using SPSS version 23. Categorical data were expressed in frequency and percentages, whereas numeric data were expressed in mean and standard deviation. The significance of the results was checked using the appropriate tests, including the independent student t-test, chi-square (or Fischer exact test if necessary), Anova test, and logistic regression. We regarded a p-value of less than 0.05 to be statistically significant.

between the sick and the control groups regarding the average education degree. There was no statistically significant difference between the other factors.

Table 2. Comparison of the sociodemographic details of the two groups.

Parameters	Rheumatoid arthritis [n = 50]		No rheumatoid arthritis [n = 50]		P-value*
	No.	%	No.	%	
Marital status					
Single	6	12.0	13	26.0	0.202
Married	44	88.0	37	74.0	
Residence					
Urban	35	70.0	33	66.0	0.668
Rural	15	30.0	17	34.0	
Education					
Illiterate	18	36.0	8	16.0	0.001
Primary school	24	48.0	11	22.0	
Secondary school	4	8.0	16	32.0	
University +	4	8.0	15	30.0	

* Chi-square test was used.

Table 3: demonstrates statistically significant differences between the R.A. patients and the control group regarding comorbidities (hypertension, diabetes mellitus).

Table 3. A comparison of the two groups comorbidities

Comorbidities*	Rheumatoid arthritis [n = 50]		No rheumatoid arthritis [n = 50]		P-value**
	No.	%	No.	%	
No	31	62.0	38	76.0	0.028
Hypertension	18	36.0	10	20.0	
DM	9	18.0	2	4.0	

*The chi-square test was employed; some individuals had more than one ailment.

Table 4: presents the incidence of depression in R.A. patients in a healthy control group. The differences between the two groups were statistically significant.

Table 4. The relation between R.A. and depression in the studied populations

Depression score [PHQ-9]	Cases "R.A."		Control "No R.A."	Odds ratio	95% C.I		P-value*
	No.	%	No.		%		
Depression PHQ-9: ≥ 5	39	78.0	22	44.0	4.51	1.89; 10.79	0.000
No Depression PHQ-9: < 5	11	22.0	28	56.0			
Total	50	100.0	50	100.0	---	---	---

* Chi-square test was used, d.f = 1.

CI=Confidence Interval, OR=Odds Ratio

Table 5 compares R.A. patients and controls concerning the intensity of depression. In 22% of R.A. patients, PHQ-9 scores were low; in 28%, it was mild; in 22%, it was moderate; in 18%, it was pretty severe; and in 10%, it was

severe. The PHQ-9 scores of the control group ranged from mild (32%), moderate (6%), severe (4%), to very severe (2%). The differences between the groups were statistically significant.

Table 5. Depression in R.A. patients compared to a control group

Depression severity [PHQ-9 score]	Cases "R.A."		Control "No R.A."		P-value*
	No.	%	No.	%	
Minimal or none (0-4)	11	22.0	28	56.0	0.001
Mild (5-9)	14	28.0	16	32.0	
Moderate (10-14)	11	22.0	3	6.0	
Moderately severe (15-19)	9	18.0	1	2.0	
Severe (20-27)	5	10.0	2	4.0	
Total	50	100.0	50	100.0	---

* Chi-square test was used, d.f = 1.

Disease activity and depression in R.A. patients are shown in Table 6. The R.A. patient with moderate disease activity had no depression, 25% had mild depression, and 25% had severe depression, based on the CDAI score. There were no patients with severe depression (37.5%), 18.8% with

mild depression (31.3%), 12.5% with moderately severe depression (31.3%), and no patients with severe depression (0%). Depression was present in 10% of patients with R.A. and high disease activity but absent in 33%, mild in 20%, moderate in 23%, moderate in 13.3%, and severe in 23.3%.

Table 6. Effect of Disease Activity on Depressive Symptoms in Patients with Rheumatoid Arthritis

Depression severity [PHQ-9 score]	Disease activity* [CDAI score] No. (%)		
	Low [2.9 – 10.0]	Moderate [10.1 – 22.0]	High [22.1 – 76.0]
Minimal or none (0-4)	2 (50.0)	6 (37.5)	3 (10.0)
Mild (5-9)	1 (25.0)	3 (18.8)	10 (33.3)
Moderate (10-14)	0 (0.0)	5 (31.3)	6 (20.0)
Moderately severe (15-19)	0 (0.0)	2 (12.5)	7 (23.3)
Severe (20-27)	1 (25.0)	0 (0.0)	4 (13.3)
Total**	4 (100.0)	16 (100.0)	30 (100.0)

* No remission case was present during data collection.

** Chi-square test is not valid to apply because six cells with low expected values

The following table will illustrate the correlation between R.A. and depression severity as measured by the PHQ-9 score, controlling for the influence of gender. Although the Mean SD of the PHQ-9 score is higher in females than males in both groups, this difference does not reach statistical significance between the patient and control groups.

Table (7) shows the correlation between R.A. and depression severity as measured by the Patient Health Questionnaire-9 (PHQ-9), controlling for the influence of gender.

Table 7. Correlation between R.A. and depression severity

Gender	Depression severity [PHQ-9 score] *		P-value**
	Rheumatoid arthritis [n = 50]	No rheumatoid arthritis [n = 50]	
Male	8.8 ± 5.3	4.0 ± 2.8	0.028
Female	10.6 ± 6.3	6.4 ± 4.7	0.007
Total	10.4 ± 6.6	52 ± 4.6	0.001

* Data are presented as Mean ± S.D.

**Independent T-test of two means was used.

5. Discussion

The purpose of this research was to characterize the incidence of depression in R.A. and to investigate the association between depression and disease activity. The study comprised 50 patients with an R.A. diagnosis and 50 healthy controls.

This research confirms the findings of a previous one by Wendlassida Joelle et al. (19), who also observed a considerably greater prevalence of depression among patients with R.A. (54%) compared to control 22(44%). Similar findings were obtained in a meta-analysis of 21 trials, including 4447 RA patients conducted by Fux et al. in China(20). Jamshidi A.R. et al. found 63.6% in a single-centre Iranian series, comparable to the data published here (21).

There are two primary arguments to explain the link between R.A. and mood disorders: One possible explanation for the co-occurrence of R.A. and depression is a shared neuroimmunological mechanism. This might be because 1

functional handicap and low quality of life can lead to the onset of depressive symptoms. A model has suggested the link between depression and psychoneuroimmunological problems. Immune system activation and the subsequent production of proinflammatory cytokines have been linked to neurochemical, neuroendocrine, and behavioral abnormalities in depression. A neurochemical mechanism claimed to be involved in severe depression is the inhibition of tryptophan (a serotonin precursor) and serotonin production, which is linked to cytokines via the activation of the enzyme indoleamine-2,3-dioxygenase (IDO). Hyperactivity of the hypothalamic-pituitary-adrenal (HPA) axis, a neuroendocrine dysfunction associated with depression, has also been related to cytokine release. Last but not least, depressive symptoms such as loss of appetite, anorexia, weight loss, exhaustion, sleep difficulties, motor retardation, lower libido, cognitive impairment, anhedonia, and sad mood are positively connected with cytokine serum levels. As a result, this model suggests that the occurrence of depression symptoms in R.A. may reflect a feature of the chronic inflammatory state of R.A.; in this instance,

depressive symptoms would be associated with cytokine release itself⁽²²⁻²⁶⁾.

Although the Mean SD of the PHQ 9 score is more significant in females than males in both groups (consistent with studies by T. PINCUS et al.⁽²⁷⁾), the prevalence of depression is still higher in R.A. than in average persons (table 7).

This study had a significant association between depression and disease activity in R.A. patients. This aligns with the study done by Kareem O et al., who found that disease activity was a significant predictor of depression in R.A. patients⁽²⁸⁾.

Regarding sociodemographic characteristics, there were significant statistical differences in education level between patients and control, while the rest of the other variables were not statistically different. Similarly, Christian A et al. reported that educational level could significantly influence R.A.'s risk and clinical course⁽²⁹⁾.

Additionally, the results of the present study showed a positive association between depression and comorbidities (hypertension and diabetes) among R.A. patients. The study of Brygida K et al. agrees with our results, which found an increase in depression symptoms in patients with R.A. and

coexisting diseases such as hypertension, hypothyroidism, hyperthyroidism, diabetes, and ischaemic heart disease⁽³⁰⁾.

The limitations of this investigation should be highlighted. The limited sample size means this research may not be typical of all patients with R.A., and more significant patient numbers were necessary for more reliable findings. In addition, patients were not followed up to show any improvement after successful therapy for R.A. The investigation was conducted at a single location, with time and resource limitations.

6. Conclusion

The Patients with rheumatoid arthritis exhibited a considerably greater incidence of depression compared to healthy controls. There is a relationship between the intensity of depression and disease activity in R.A. patients. A substantial direct relationship exists between poor educational level, depression, and comorbidities. The researcher recorded that Depressive symptoms are widespread in people with R.A. and should thus be recognized while assessing this rheumatological condition. Further research with a bigger sample size and a longer length of follow-up is proposed to notice comparable results and ascribe higher relevance to them.

References

- [1] Jeffery RC. Clinical features of rheumatoid arthritis. *Medicine (Baltimore)* 2014;42:231–6.
- [2] Firestein GS et al., *Etiology and Pathogenesis of Rheumatoid Arthritis. Kelley and Firestein's Textbook of Rheumatology*, 10th edition, Elsevier, 2017.
- [3] Kyla A McKay et al., "Psychiatric Comorbidity is Associated with Disability Progression in multiple sclerosis," *Neurology*, vol. 90, no. 15, pp. 1316-1323, 2018. *Crossref*, <https://doi.org/10.1212/WNL.0000000000005302>
- [4] Kojima Masayo et al., "Depression, Inflammation, and Pain in Patients with Rheumatoid Arthritis," *Arthritis Care & Research*, vol. 61, no. 8, pp. 1018-1024, 2009. *Crossref*, <https://doi.org/10.1002/art.24647>
- [5] Rinie Geenen et al., "Psychological Interventions for Patients with Rheumatic Diseases and Anxiety Or Depression," *Best practice & Clinical research rheumatology*, vol. 26, no. 3, pp. 305-319, 2012. *Crossref*, <https://doi.org/10.1016/j.berh.2012.05.004>
- [6] Brygida Kwiatkowska et al., "Factors of Depression Among Patients with Rheumatoid Arthritis," *Reumatologia*, vol. 56, no. 4, pp. 219-227, 2018. *Crossref*, <https://doi.org/10.5114/reum.2018.77973>
- [7] E Yelin, "Work Disability in Rheumatoid Arthritis: Effects of The Disease, Social, and Work Factors," *Annals of Internal Medicine*, vol. 93, no. 4, pp. 551-556, 1980. *Crossref*, <https://doi.org/10.7326/0003-4819-93-4-551>
- [8] Anthony S. Fauci, Carol A. Langford, *Rheumatoid Arthritis. Harrison's Rheumatology*, 4th edition. McGraw-Hill Education, 2017.
- [9] O'Dell JR et al., *Rheumatoid Arthritis. Current Diagnosis and Treatment Rheumatology*, 3rd Edition, The McGraw-Hill Education, 2013.
- [10] Francesca Angelotti, "One year in review 2017: Pathogenesis of Rheumatoid Arthritis," *Clinical and Experimental Rheumatology*, vol. 35, no. 3, pp. 368-378, 2017.
- [11] jinpiao Lin et al., "Datasets of YY1 Expression in Rheumatoid Arthritis Patients," *Data in Brief*, vol. 9, pp. 1034-1038, 2016. *Crossref*, <https://doi.org/10.1016/j.dib.2016.11.046>
- [12] Lee Goldman, and Andrew I. Schafer, *Goldman-Cecil medicine*, Elsevier, vol. 2, 26th Edition, 2020.
- [13] Ralston SH, McInnes IB., *Davidson's Principles and Practice of Medicine, Rheumatology and bone disease*, 22nd edition Elsevier Churchill Livingstone. 2014.
- [14] Cynthia S. Crowson et al., "The Lifetime Risk of Adult-Onset Rheumatoid Arthritis and Other Inflammatory Autoimmune Rheumatic Diseases," *Arthritis & Rheumatism*, vol. 63, no. 3, pp. 633-639, 2011. *Crossref*, <https://doi.org/10.1002/art.30155>

- [15] Daniel Aletaha et al., “2010 Rheumatoid Arthritis Classification Criteria: An American College of Rheumatology/European League Against Rheumatism Collaborative Initiative,” *Arthritis & Rheumatism*, vol. 62, no. 9, pp. 2569-2581, 2010. *Crossref*, <https://doi.org/10.1002/art.27584>
- [16] Lucas Francisco Botequiao Mella, Manoel Barros Bértolo, and Paulo Dalgalarrodo, “Depressive symptoms in Rheumatoid Arthritis,” *Brazilian Journal of Psychiatry*, vol.32 no.3, pp. 257-263, 2010. *Crossref*, <https://doi.org/10.1590/s1516-44462010005000021>
- [17] K Kroenke, RL Spitzer, and J B Williams, “The PHQ-9: Validity of a Brief Depression Severity Measure,” *Journal of general Internal Medicine*, vol. 16, no. 9, pp. 606-613, 2001. *Crossref*, <https://doi.org/10.1046/j.1525-1497.2001.016009606.x>
- [18] D Aletaha, and J Smolen, “The Simplified Disease Activity Index (SDAI) and the Clinical Disease Activity Index (CDAI): a review of their usefulness and validity in Rheumatoid Arthritis,” *Clinical and experimental Rheumatology*, vol. 23, no. 5, pp. 100-108, 2005.
- [19] Wendlassida Joelle Tiendrébéogo Zabsonre et al., “Frequency and Factors Associated with Depression in Rheumatoid Arthritis in African Black Patients: Case Control Study,” *Open Journal of Rheumatology and Autoimmune Diseases*, vol. 9, no. 2, pp. 35-41, 2019. *Crossref*, <https://doi.org/10.4236/ojra.2019.92004>
- [20] Xin Fu et al., “The Prevalence of Depression in Rheumatoid Arthritis in China: A Systematic Review,” *Oncotarget*, vol. 8, no. 32, pp. 53623-53630, 2017. *Crossref*, <https://doi.org/10.18632/oncotarget.17323>
- [21] Ahmad-Reza Jamshidi et al., “Anxiety and Depression in Rheumatoid Arthritis: An Epidemiologic Survey and Investigation of Clinical Correlate in Iranian Population,” *Rheumatology International*, vol. 36, no. 8, pp. 1119-1125, 2016. *Crossref*, <https://doi.org/10.1007/s00296-016-3493-4>
- [22] Olga J G Schiepers, Marieke C Wichers, and Michael Maes, “Cytokines and Major Depression,” *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, vol. 29, no. 2, pp. 201-17. *Crossref*, <https://doi.org/10.1016/j.pnpbp.2004.11.003>
- [23] Kenneth R Kaufman, “Etanercept, Anticytokines, and Mania,” *International clinical psychopharmacology*, vol. 20, no. 4, pp. 239-41, 2005. *Crossref*, <https://doi.org/10.1097/00004850-200507000-00008>
- [24] Kai G Kahl et al., “Cortisol, the Cortisol-Dehydroepiandrosterone Ratio, and Proinflammatory Cytokines in Patients with Current Major Depressive Disorder Comorbid with A Borderline Personality Disorder,” *Biological Psychiatry*, vol. 59, no. 7, pp. 667-671, 2006. *Crossref*, <https://doi.org/10.1016/j.biopsych.2005.08.001>
- [25] David B Weiss et al., “Psychiatric Manifestations of Autoimmune Disorders,” *Current treatment options in neurology*, vol. 7, no. 5, pp. 413-417, 2005.
- [26] Anisman Hymie et al., “Cytokines as a Precipitant of Depressive Illness: Animal and Human Studies,” *Current pharmaceutical design*, vol. 11, no. 8, pp. 963-972. 2005. *Crossref*, <https://doi.org/10.2174/1381612053381701>
- [27] T. Pincus et al., “Prevalence of self-reported Depression in Patients with Rheumatoid Arthritis. Rheumatology,” *The British Journal Of Rheumatology*, vol. 35, no. 9, pp. 879-83, 1996. *Crossref*, <https://doi.org/10.1093/rheumatology/35.9.879>
- [28] Owais Kareem et al., “Frequency of Depression in Patients with Rheumatoid Arthritis,” *The Professional Medical Journal*, vol. 27, no. 3, pp. 646-650, 2020. *Crossref*, <https://doi.org/10.29309/TPMJ/2020.27.03.4242>
- [29] Christian Adrián López-Castillo et al., “Impact of Educational Level on Rheumatoid Arthritis: A Systematic Review,” *Revista Colombiana Rheumatologia*, vol. 21, no. 4, pp. 201–212, 2014. *Crossref*, <https://doi.org/10.1016/j.rcreu.2014.09.002>
- [30] Brygida Kwiatkowska et al., “Factors of Depression Among Patients with Rheumatoid Arthritis,” *Reumatologia*, vol. 56, no. 4, pp. 219-227, 2018, *Crossref*, <https://doi.org/10.5114/reum.2018.77973>