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Characteristics of depressive disorders in patients with rheumatoid arthritis and some related factors

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Abstract. – OBJECTIVE: Rheumatoid arthritis (RA), a type of chronic arthritis, is common in Vietnam. It has severe consequences for patients, both physically and psychologically, including depressive disorders. Therefore, early detection of depressive disorders is of high importance to help provide comprehensive treatment and improve RA patients' quality of life. This cross-sectional study explored the prevalence of depressive disorders and their salient characteristics and related factors in RA patients in Vietnam.

PATIENTS AND METHODS: We enrolled 156 patients diagnosed with RA using the ACR-1987 criteria. The Patient Health Questionnaire-9 (PHQ-9) was used to screen for depressive disorders. Patients' demographic characteristics and clinical and laboratory investigation results, such as the visual analog score, complete blood count, erythrocyte sedimentation rate, Disease Activity Score 28 for RA with C-reactive protein (DAS28-CRP), and quality-of-life score (based on the SF-36 test) were analyzed. Depressive disorders assessed on the first day of admission were reevaluated by a psychiatrist if the PHQ-9 score was ≥ 5.

RESULTS: According to the PHQ-9 results, depression prevalence among RA patients was 76.3%. The majority of patients (49.4%) had moderate-to-severe depression and 91% experienced sleep disorder symptoms. Negative thoughts – suicidal ideation or self-injury – were reported by 21.8% of patients. Depression severity had a moderately positive relationship with disease activity level and a moderately negative relationship with quality of life.

CONCLUSIONS: Depression prevalence was high among RA patients. Depression severity increased with disease activity and decreased quality of life.

Key Words:
Rheumatoid arthritis, Depression, PHQ-9, DAS28-CRP, SF-36.

Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory joint-involved disease that afflicts 0.5 - 1% of the population worldwide and 0.17 - 0.3% of the population of Asian countries[1,2]. It is characterized by chronic inflammation of the synovia, which gradually causes cartilage and subchondral bone destruction. This progression leads to joint adhesion and deformity and finally contributes to disability at various levels[2]. In addition to chronic synovial inflammation, patients with RA are more likely to suffer from harmful psychological consequences. Persistent pain, functional disabilities, fatigue, economic burden, and drug side effects severely impair patients' quality of life (QoL)[3,4]. Therefore, psychological disorders, especially depression, are relatively common among patients with RA. Although the importance of regulating these conditions, e.g., stress and depression, in RA has been extensively studied, depression has not received sufficient research attention[5].

Patients with RA are twice to four times as likely to develop depressive disorders as members of the general population[6]. Depression in RA leads to an increased burden on both patients and society[7]. Early detection and diagnosis of depression in RA is of great importance in order to contribute to comprehensive treatment, improve patients' outcomes and QoL, and prevent disease aggravation.

Therefore, we conducted a survey of depressive disorders in RA patients using the Patient Health Questionnaire-9 (PHQ-9) and evaluated the main characteristics and factors related to depression in this group of patients. The PHQ-9, which objectifies and assesses the degree of severity of depression in RA patients, is applied in many countries around the world[8]. It has also been standardized

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and widely used in mental health institutions in Vietnam. The results of our study may help rheumatologists gain a more comprehensive view of RA patients, detect depressive disorders early for timely treatment, and improve patients' outcomes.

Patients and Methods

Study Location

This cross-sectional study selected participants from among RA patients treated at the Department of Rheumatology of Bach Mai Hospital between July 2018 and August 2019. Rheumatoid arthritis was diagnosed based on the ACR-1987 criteria. Depressive disorders were assessed by the PHQ-9 on the first day of admission to the Rheumatology Department and reevaluated at the Psychiatry department by a psychiatrist if the PHQ-9 score was ≥ 5. Patients with a past medical history of mental illness and severe chronic comorbidities - malignancy, heart failure, kidney failure, or serious pulmonary diseases - were excluded.

Data Collection

The patients' demographic characteristics, results of clinical and laboratory investigations, including the visual analog score (VAS), complete blood count, erythrocyte sedimentation rate, Disease Activity Score 28 for RA with C-reactive protein (DAS28-CRP), and QoL score (SF-36 test) were analyzed. These data were collected at Bach Mai Hospital and compared with reference parameters published by the respective departments. Depressive disorders were assessed by the PHQ-9 on the first day of hospitalization. The maximum total score in this questionnaire was 27, and a score of ≥ 5 points was classified as depression. Patients with a total score ≥ 5 were reassessed by a psychiatrist. Researchers also evaluated some depression-related factors of RA, such as age, gender, age of onset, duration of disease, VAS score, disease stage, disease activity level, and QoL.

Consistency of Research Results

Relevant research information was collected for every patient using the same medical record form. Laboratory tests were performed using standard test kits at Bach Mai Hospital. At the Department of Rheumatology, a rheumatologist applied the PHQ-9 questionnaire to directly gather data and screen for depression in RA patients, while in the Psychiatry department of Bach Mai Hospital, a psychiatrist conducted a reassessment of depression.

Statistical Analysis

Statistical analysis was performed using SPSS v. 20.0 (IBM Corp., Armonk, NY, USA) package program. Descriptive statistics for demographic and clinical characteristics are presented. Frequencies and percentages are given for qualitative variables, while medians and interquartile ranges are given for quantitative ones. The association between depression and some factors was analyzed. A p-value < 0.05 was considered statistically significant.

Results

We enrolled 156 patients with RA who met the study criteria. Table I shows the primary baseline characteristics of the study sample. The average age of the patients was 57.1 years. Females comprised the majority (90.4%). The mean duration of the disease was 6.78 years. The mean VAS score at the time of admission was 4.03 (range 0-8). The average disease activity score (DAS28-CRP score) of 3.7 ± 1.23 indicated a moderate level of activity. Most patients had a moderate QoL (SF-36 score of 40.12).

The majority of RA patients (n = 119, 76.3%) were classified as having depression, as determined by the PHQ-9. After a psychiatric reevaluation, 60.9% of these individuals had depression (Figure 1).

Table II shows that approximately 27% of RA patients experienced mild symptoms of depression. A relatively high proportion of patients (49.4%) suffered from moderate-to-severe manifestations of depressive disorders. Ten patients, in particular, had severe depression (6.4%).

Table III shows that the most common symptom among the manifestations of depression

Table I. General characteristics of the study population of patients with rheumatoid arthritis (n = 156).

Characteristics	Mean ± SD (range)
Age (years)	57.1 ± 10.8 (21 - 75)
Age of disease onset (years)	50.3 ± 13.5 (7 - 86)
Sex (male/female)	9.6% / 90.4%
BMI (kg/m^2)	20.9 ± 2.37 (14.2 - 28.1)
Duration of disease (years)	6.78 ± 7.32 (0 - 30)
Duration of morning stiffness (minutes)	58 ± 31.6 (10 - 150)
VAS score	4.03 ± 1.94 (0 - 8)
DAS28-CRP score	3.7 ± 1.23 (1.03 - 6.46)
SF-36 score	40.12 ± 14.26

SD: Standard deviation; BMI: Body mass index, VAS: Visual Analogue Scale, DAS28-CRP: DAS28-CRP: Disease Activity Score 28 using C-reactive protein, SF-36: 36-Item Short Form Survey.

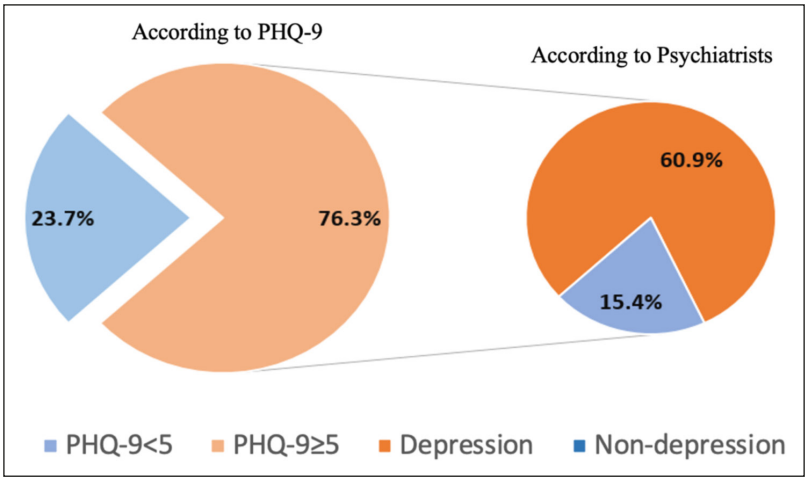

Figure 1. The prevalence of depression among patients with rheumatoid arthritis (n = 156).

was "trouble falling asleep, staying asleep, or sleeping too much" (91%), followed by "feeling tired or having little energy" (76.9%). In addition, 21.8% of patients had negative thoughts – suicidal ideation or self-injury. The most severe symptom was sleep-related disorders, with an average score of 1.69 ± 0.913.

As shown in Table IV, there was no age, age of RA onset, or sex differences between the two groups (with depression vs. without depression). Patients with depression suffered from longer RA duration than patients without depression, but this was not a significant difference. In the with-depression group, both the duration of morning stiffness and VAS score were greater than those of the without-depression group, and these differences were statistically significant ($p < 0.05$).

Figure 2 shows that there was a moderate positive relationship between the severity of depressive disorders and RA activity level ($r = 0.595$, $p < 0.001$).

Table II. Depression severity in patients with rheumatoid arthritis according to the Patient Health Questionnaire-9 (PHQ-9; n = 156).

PHQ-9 score	n	%
None (0 - 4)	37	23.7
Mild (5 - 9)	42	26.9
Moderate (10 - 14)	37	23.7
Moderately severe (15 - 19)	**30**	**19.2**
Severe (20 - 27)	**10**	**6.4**
Total	156	100%
Mean ± SD (range)	10.01 ± 6.15 (0 - 26)	

SD: Standard deviation.

Table III. Symptoms of depression in patients with rheumatoid arthritis (n = 156).

	Symptom	n	%	Mean ± SD score (from a range of 0 to 3)
1	Little interest or pleasure in doing things	104	66.7%	1.10 ± 0.995
2	Feeling down, depressed, or hopeless	109	69.9%	1.25 ± 1.057
3	Trouble falling asleep, staying asleep, or sleeping too much	**142**	**91%**	**1.69 ± 0.913**
4	Feeling tired or having little energy	120	76.9%	1.24 ± 0.931
5	Poor appetite or overeating	102	56.4%	1.05 ± 0.962
6	Feeling bad about oneself or that one is a failure or has let oneself or one's family down	106	67.9%	1.15 ± 0.982
7	Trouble concentrating on things, such as reading the newspaper or watching television	95	60.9%	0.78 ± 0.724
8	Moving or speaking so slowly that other people could have noticed, or the opposite, being so fidgety or restless to have been seen as moving around a lot more than usual	118	75.6%	1.10 ± 0.821
9	Thoughts that one would be better off dead or of hurting oneself in some way	**34**	**21.8%**	**0.53 ± 0.731**

SD: Standard deviation.

Table IV. Depression and some related factors in patients with rheumatoid arthritis (RA).

	With-depression group (n = 119)	Without-depression group (n = 37)	*p*-value
Mean age (years)	56.65 ± 8.2	57.22 ± 11.53	0.74
Sex Male	73.33%	26.67%	0.781
Female	81.56%	18.44%	
Age of RA onset (years)	50.7 ± 13.12	49.97 ± 10.59	0.2
Duration of RA (years)	6.82 ± 7.2	6.65 ± 7.79	0.474
Duration of morning stiffness (minutes)	**65.13 ± 38.85**	**33.78 ± 36.69**	0.01
VAS score	4.75 ± 1.85	2.11 ± 1.54	0.026

$p < 0.05$ is considered statistically significant for the Student's *t*-test. RA: Rheumatoid arthritis, VAS: Visual Analogue Scale.

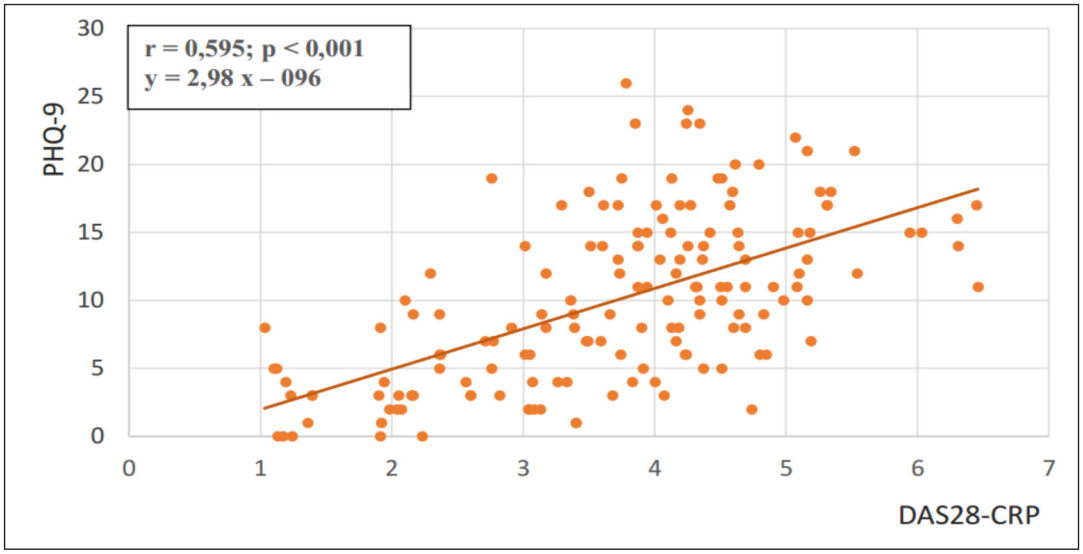

Figure 2. Linear regression between the severity of depressive disorders based on the PHQ-9 score and rheumatoid arthritis activity measured by the DAS28-CRP score (n = 156).

There was a moderate negative relationship between the severity of depressive disorders and the QoL score (r = -0.67; $p < 0.001$; Figure 3).

The mean total SF-36 score of the eight indices for the with-depression group (33.28 ± 11.94) was lower than that for the without-depression group (50.43 ± 9.97). This difference was statistically significant ($p < 0.01$). The scores of all eight domains were significantly lower in the with-depression group than in the without-depression group (Figure 4). Among these domains, general health and emotional well-being were the most markedly different ($p < 0.01$).

Discussion

The results of the PHQ-9 indicated that 76.3% of the 156 RA patients had symptoms of depression, with moderate-to-severe depression being of relatively high prevalence (49.4%) and 21.8% of the patients enduring severe manifestations. 38.8% of participants in a 2013 meta-analysis by Matcham et al[9] of 72 UK studies with 13,000 RA patients reported having moderate-to-severe depressive symptoms. This was a smaller proportion of patients than in our study, which might be explained by the fact that RA patients in the UK receive better medical care as well as more comprehensive management and treatment. Ionescu et al[10] indicated that the prevalence of depression in RA was 2 to 3 times higher than the prevalence in the general population, with a meta-analysis reporting that 16.8% of RA patients had a major depressive disorder. The pathogenesis of depression in RA remains to be fully understood, but recent literature suggests that immune-mediated processes are involved and that there are similarities between the neural

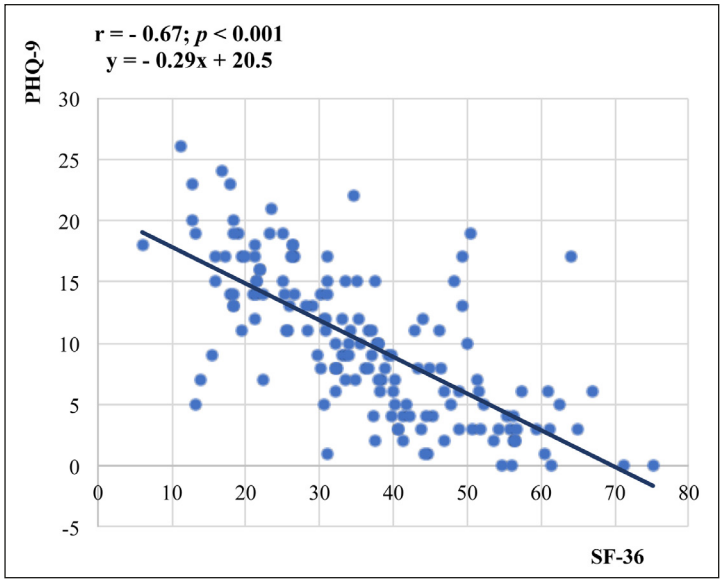

Figure 3. The relationship between severity of depression based on the PHQ-9 score and patients' quality of life according to the SF-36 score (n = 156).

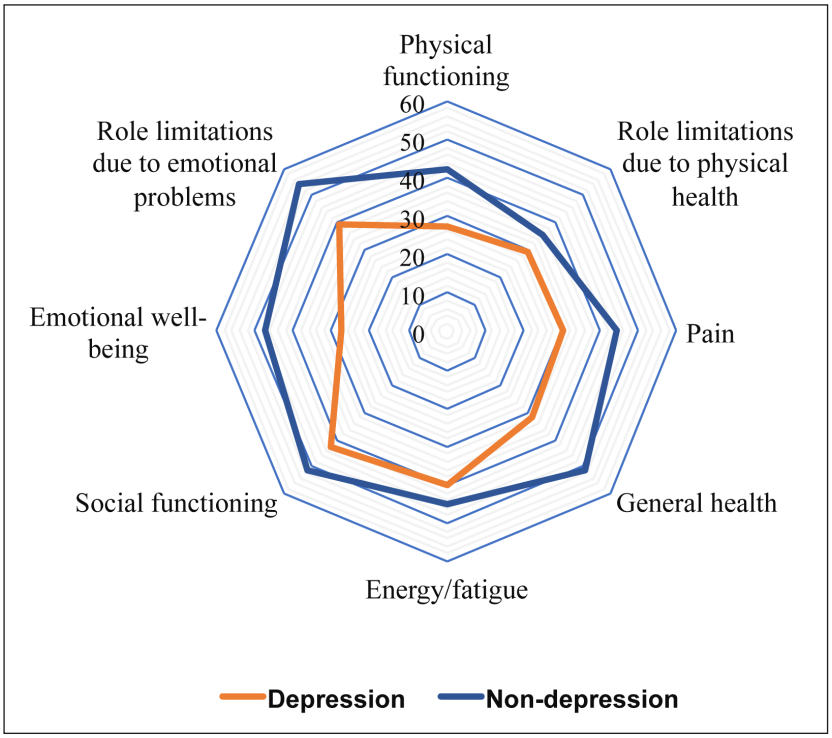

Figure 4. Quality of life domains in the SF-36 questionnaire (n = 156).

networks recruited in inflammation and those implicated in the pathophysiology of depression[10].

In our study, 119 patients with a PHQ-9 score ≥ 5 were reevaluated by psychiatrists, and finally, 95 participants were given a diagnosis of depression. Thus, the prevalence of depression after reassessment was 60.9%. This result was consistent with that of the PHQ-9, which has been demonstrated by many studies[11] to be reliable and is widely applied globally. In the case of depression in RA, Hitchon et al[12] found that although depression screening instruments, including the PHQ-9, showed good diagnostic performance, their diagnoses warranted clinical confirmation. Kroenke et al[13] used the PHQ-9 to interview patients without psychiatric intervention and showed that the instrument was reliable in detecting depression, with Cronbach's alpha of 0.89, a sensitivity of 84%, and a specificity of 72%.

Although the pathogenesis of depressive disorders in RA remains to be clearly understood, research in this area is increasing. RA is a chronic disease with a complicated process, leading to serious consequences so RA patients are more prone to both physical and mental injuries[7]. Reduced engagement in leisure and social activities has been shown to significantly raise the risk of depression. The co-existence of depression and RA intensifies the burden on the healthcare system, on rheumatologists in particular, and general practitioners in general. Depression in rheumatoid arthritis may be caused by damage to central and peripheral nerves due to inflammatory factors and autoantibodies generated by biochemical changes. Increased secretion of tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) increases the levels of Corticotropin Releasing Hormone (CRH), Adrenocorticotropic Hormone (ACTH), and cortisol, leading to dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, causing depressive symptoms. The specific mechanism involves TNF-α stimulating the enzyme indoleamine 2,3-dioxygenase, which causes the degradation of tryptophan (a precursor of serotonin synthesis), leading to reduced serotonin levels. Proinflammatory cytokines that can affect the central nervous system, such as TNF and IL-1, act directly on the hippocampus as well as on the HPA axis. Although some cytokines do not cross the blood-brain barrier, they can affect the central nervous system through the second messengers, IL-6, and IL-12. Specifically, IL-6 activates the HPA axis and increases cortisol metabolism, while IL-12 promotes the immune-mediated systemic inflammatory response, causing a Th1/Th2 imbalance and increasing neuronal degeneration, leading to symptoms of depression[14].

Depressive disorders in patients with RA have various manifestations. Common symptoms include fatigue, pain, weakness, loss of appetite, negative thoughts about illness, diminishment or loss of interest, depressed mood, boredom, weight loss, and impulsive thoughts[9]. In our study, the frequent symptoms according to the PHQ-9 were "trouble falling asleep, staying asleep, or sleeping too much" (91%) and "feeling tired or having little energy" (79.6%). Thirty-four patients (21.8%) had negative thoughts such as suicidal ideation or showed self-harming behaviors. These dangerous and life-threatening manifestations should be noticed and detected early when physicians examine patients in order to provide timely, comprehensive, and effective treatment. The symptom "trouble falling asleep, staying asleep, or sleeping too much" was the most severe, with a mean score of 1.69 ± 0.913. This obvious manifestation, which indicates possible depression in RA patients, can be promptly discovered.

Low socioeconomic status, sex, age, race, functional limitations, pain status, and severe clinical symptoms are all associated with depression in RA[6]. In our study, there was no difference in mean age, mean age at disease onset, and mean disease duration between the with-depression group and the without-depression group ($p > 0.05$). Duration of morning stiffness, mean VAS score and DAS28-CRP score were significantly higher in the depressive patients than in the non-depressive patients ($p < 0.01$). In particular, there was a close association between the severity of depression according to the PHQ-9 score and the degree of disease activity measured by the DAS28-CRP score. The higher the degree of disease activity, the higher the severity of depressive disorders. There was a moderate positive correlation between disease activity level and severity of the depressive disorder ($r = 0.595$, $p < 0.001$). Similarly, Imran et al[2] conducted a study of 102 RA patients which showed that the prevalence of depressive disorders (75%) was closely related to the degree of disease activity ($r = 0.615$; $p < 0.000$).

Many cytokines, such as TNF-α, IL-23, IL-17A, IL-1, IL-6 induce systemic and local inflammatory responses, causing flares or exacerbating disease in RA patients. IL-6 has been shown to play an important role in the pathogenesis of depression. It has consistently been found to be elevated in patients with stress and depression. Blood levels of IL-6 are related to subtypes, clinical features, treatment response, and prognosis of depression. Therefore, inflammation control may be a new antidepressant therapy effective for treating depressive disorders in RA[15].

Our study found that there was a negative relationship between depression severity and QoL ($r = -0.68$; $p < 0.001$). Katchamart et al[16] showed that high disease activity levels, as well as depressive disorders, had an extremely negative impact on the QoL of RA patients. Sruamsiri et al's study[17] showed that despite advancements in RA treatment, the extra-articular burden, including multiple comorbidities and psychosocial impairment, remained substantial. RA is associated with fatigue, depression, cognitive dysfunction, reduced work performance, lower productivity, and worsened QoL. According to Ionescu et al[10], depression is one of the most fre-

quent comorbidities of RA; it takes a high toll on the QoL of patients and also leads to decreased life expectancy. Depression in patients with RA is associated with poor long-term outcomes. It alters treatment compliance, causes more comorbidities, and leads to higher mortality, partly through increased risk of suicide. It also increases health service use and healthcare costs directly through hospitalization, as well as indirectly through loss of work productivity[10]. Li et al's study[18] evaluating the economic burden of depression among adults with RA in the United States found increased use of healthcare, loss of work productivity, and a high economic burden among RA patients due to comorbid depression. These findings emphasize the importance of managing depression and including depression as a factor when devising treatment algorithms for patients with RA[18,19]. Assessment of depression could be a significant psycho-marker of rheumatological outcome in RA.

Lastly, our research demonstrated that PHQ-9 is useful for screening purposes for the presence of a current major depressive episode. Having said that, this quick assessment tool only consists of a relatively small number of questions, which aims to identify depression. Besides, due to the lack of clear pathophysiological diagnostic indicators, the identification of depression disorders has historically been challenging. Therefore, the use of PHQ-9 for diagnostic purposes is not supported in the context of a psychiatric clinic due to its low specificity and low positive predictive value. More crucially, we conducted clinical interviews in which we broadly questioned patients to learn what they were thinking; yet it was incredibly perplexing to comprehend their inner reality and the restrictions brought on by the functional impairment. It is assumed that each person's experience, social and personal history, and worldview will have a varied impact on how such an impairment affects them. A total psycho-physical structural subversion seemed to be overpowering the patient's thought so that he/she could suffer from a devastating state without being classified into any documented psychological disorders if doctors did not look deeply into the patient's mind but focused only on scores on paper.

Lastly, it is crucial to underscore that to prevent patients from feeling demoralized when observing the transformation of their pathological condition, which may take a turn for the worse, and potentially lead to a significant disruption in their functioning due to a state of psychological alteration, active "listening" becomes imperative[20].

Conclusions

The severity of depressive disorder, based on the PHQ-9 score, was high in patients with RA. Moderate-to-severe depression had a relatively high prevalence among RA patients, and 21.8% of patients endured severe manifestations with negative thoughts such as suicidal ideation or self-injury. The level of depressive disorder was higher with increasing RA activity, while it was lower with increasing QoL.

Authors' Contributions

Pham Hoai Thu and Nguyen-Van Hung prepared, drafted, and revised the manuscript critically, for important intellectual content. Pham Hoai Thu and Nguyen-Van Hung contributed substantially to the acquisition, analysis, and interpretation of data. Each author gave final approval to the version of the manuscript submitted for publication and agreed to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethics Approval

This study was approved by the Institution Review Board of Hanoi Medical University and the Institutional Review Board at Dinh Tien Hoang Institute of Medicine (Issued date 30 June 2018/ IRB -1800).

Informed Consent

Informed consent was obtained from all participants.

Data Availability

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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None.

Conflicts of Interest

There are no conflicts of interest to declare.

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References

1) Gibofsky A. Epidemiology, pathophysiology, and diagnosis of rheumatoid arthritis: A Synopsis. Am J Manag Care 2014; 20: S128-S135.

2) Imran MY, Saira Khan EA, Ahmad NM, Farman Raja S, Saeed MA, Ijaz Haider I. Depression in Rheumatoid Arthritis and its relation to disease activity. Pak J Med Sci 2015; 3: 393-397.
3) Pollard L, Choy EH, Scott DL. The consequences of rheumatoid arthritis: quality of life measures in the individual patient. Clin Exp Rheumatol 2005; 23: S43-S52.
4) Sheehy C, Murphy E, Barry M. Depression in rheumatoid arthritis--underscoring the problem. Rheumatology (Oxford) 2006; 45: 1325-1327.
5) Murray CJ, Lopez AD, Jamison DT. The global burden of disease in 1990: summary results, sensitivity analysis and future directions. Bull World Health Organ 1994; 72: 495-509.
6) Margaretten M, Julian L, Katz P, Yelin E. Depression in patients with rheumatoid arthritis: description, causes and mechanisms. Int J Clin Rheumtol 2011; 6: 617-623.
7) Dickens C, Creed F. The burden of depression in patients with rheumatoid arthritis. Rheumatology (Oxford) 2001; 40: 1327-1330.
8) Krug HE, Woods SR, Mahowald ML. The importance of identifying depression in patients with rheumatoid arthritis: evaluation of the beck depression inventory. J Clin Rheumatol 1997; 3: 248-257.
9) Matcham F, Rayner L, Steer S, Hotopf M. The prevalence of depression in rheumatoid arthritis: a systematic review and meta-analysis. Rheumatology (Oxford) 2013; 52: 2136-2148.
10) Ionescu CE, Popescu CC, Agache M, Dinache G, Codreanu C. Depression in Rheumatoid Arthritis: A Narrative Review-Diagnostic Challenges, Pathogenic Mechanisms and Effects. Medicina (Kaunas) 2022; 58: 1637.
11) Huang FY, Chung H, Kroenke K, Delucchi KL, Spitzer RL. Using the Patient Health Questionnaire-9 to Measure Depression among Racially and Ethnically Diverse Primary Care Patients. J Gen Intern Med 2006; 21: 547-552.
12) Hitchon CA, Zhang L, Peschken CA, Lix LM, Graff LA, Fisk JD, Patten SB, Bolton J, Sareen J, El-Gabalawy R, Marriott J, Bernstein CN, Marrie RA. Validity and Reliability of Screening Measures for Depression and Anxiety Disorders in Rheumatoid Arthritis. Arthritis Care Res (Hoboken) 2020; 72: 1130-1139.
13) Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med 2001; 16: 606-613.
14) Capuron L, Dantzer R. Cytokines and depression: the need for a new paradigm. Brain Behav Immun 2003; 17: S119-S124.
15) Ting EYC, Yang AC, Tsai SJ. Role of Interleukin-6 in Depressive Disorder. Int J Mol Sci 2020; 21: 2194.
16) Katchamart W, Narongroeknawin P, Chanapai W, Thaweeratthakul P. Health-related quality of life in patients with rheumatoid arthritis. BMC Rheumatol 2019; 3: 34.
17) Sruamsiri R, Kaneko Y, Mahlich J. The underrated prevalence of depression in Japanese patients with rheumatoid arthritis - evidence from a Nationwide survey in Japan. BMC Rheumatol 2017; 1: 5.
18) Li N, Chan E, Peterson S. The economic burden of depression among adults with rheumatoid arthritis in the United States. J Med Econ 2019; 22: 372-378.
19) Fakra E, Marotte H. Rheumatoid arthritis and depression. Joint Bone Spine 2021; 88: 105200.
20) Basile G. The autobiographical narrative as a damage assessment means: injuries to profound subjective sensitivities - personalization and objectivization of medicolegal relevance. Clin Ter 2022; 173: 585-589.