ADDIS ABABA UNIVERSITY COLLEGE OF HEALTH SCIENCES

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Prevalence and Factors Associated with Anxiety and Depression in Rheumatoid Arthritis Patients: A Multi-Center Cross-Sectional Study in Addis Ababa, Ethiopia

A research thesis submitted to the College of Health Sciences, department of internal medicine, presented in partial fulfillment of the requirements for a specialty certificate in internal medicine

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Abstract

Background: Rheumatoid arthritis (RA) is a chronic inflammatory disorder that affects both physical and mental health. Depression and anxiety are common comorbidities among RA patients, which may impact disease outcomes and quality of life. However, there is limited data in Ethiopia.

Objective: To determine the prevalence of anxiety and depression among RA patients in Addis Ababa, Ethiopia, and to explore the factors contributing to these mental health disorders.

Methods: This was a multicenter cross-sectional study conducted among RA patients who had follow up at rheumatology clinics in Addis Ababa, Ethiopia. Data was collected using chart review and interviews. The estimated sample size was 308. A convenient sampling technique was employed to recruit study participants. Depression and anxiety were assessed using the Patient Health Questionnaire (PHQ-9) and the Generalized Anxiety Disorder Scale (GAD-7). Data entry, data cleaning, and analysis were conducted using the SPSS 27.1. Binary logistic regression analysis was used to identify factors associated with depression and anxiety.

Results: The mean age of the participants was 51.18 years (±13.05), with 86.3% female. The prevalence of depression and anxiety among the RA patients was 39.9% and 32.4%, respectively. In multivariable logistic regression female sex (AOR = 5.13; 95% CI: 1.87–14.0; p = 0.001), poor medication adherence (AOR = 6.59; 95% CI: 2.35–18.4; p < 0.001), moderate to severe disability (AOR = 3.96; 95% CI: 2.15–7.31; p < 0.001), severe to very severe disability (AOR = 6.66; 95% CI: 1.82–24.3; p = 0.004), and high disease activity (AOR = 3.26; 95% CI: 1.60–6.63; p = 0.001) were all independently associated with increased odds of depression and anxiety.These factors were also independently associated with anxiety among RA patients, although with a lower odds ratio than that found for depression.

Conclusion and recommendation: Depression and anxiety are highly prevalent among RA patients, and disease-related factors such as disease activity, poor medication adherence and disability are major contributors to mental health burden. Mental health screening should be an integral part of RA that underscores the need for comprehensive management to improve overall patient care and outcomes.

Keywords: RA, depression, anxiety, Ethiopia

Table of Content

List of Table

List figures

ACRONYME AND ABRIVATION

AAU-Addis Ababa University

CHS-college of health science

DAS-28-Disease activity score-28

DMARDS-Disease-modifying anti-rheumatic drug

GAD 7- Generalized Anxiety Disorder–7

HADS–Hospital anxiety and depression

MMAS-4-Morisky medication adherence–4

PHQ-9-patient health questionnaire-9

PGA-patient global assessment

RA-Rheumatoid arthritis

1. Introduction

1.1 Background

Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by unresolved synovial inflammation with tissue-destructive consequences. It remains one of the leading causes of disability and labor loss, affecting approximately 0.2-1% of the global population(1).

Beyond the physical manifestations, RA is frequently associated with poor health outcomes and increased mortality. In addition to recurrent pain, fatigue, and increased rates of physical disability, people with rheumatoid arthritis (RA) have a higher prevalence of some mental health disorders, particularly mood disorders(2,3).

Studies have consistently demonstrated a higher prevalence of anxiety and depression in individuals with RA than in the general population(4). This area has been the focus of research to improve RA prevention and treatment. Rheumatologists face challenges in detecting anxiety and depression symptoms in ambulatory care settings. This study used PHQ9 and GAD7 score, to assess anxiety and depression symptoms in RA patients respectively. Questionnaires are difficult to administer in everyday medical settings due to the burden they place on patients and the time required(5).

In Ethiopia, little research has been done on the incidence and correlations of anxiety and depression in RA patients. Understanding the unique challenges that people with RA face in this context is critical for creating culturally appropriate interventions and improving mental health outcomes.

The study's findings will help to improve understanding of the psychological burden of RA in Ethiopia, as well as inform the development of targeted interventions to address patients' mental health concerns. Furthermore, this study will help healthcare providers and policymakers develop comprehensive care plans for people with RA.

By addressing the factors associated with anxiety and depression in RA, we can improve patients' overall quality of life while also reducing the disease's negative impact. This study is an important step toward improving mental health care for people with RA in Ethiopia.

1.2 Statement of the problem

Rheumatoid arthritis is a chronic autoimmune illness that causes joint inflammation, discomfort, and stiffness. Aside from its physical symptoms, RA can have a substantial impact on patients' mental health, causing a variety of psychological problems, such as anxiety and sadness. These mental health disorders can have a major impact on RA patients' quality of life, everyday functioning, and illness burden.

Studies examining the prevalence and factors linked to anxiety and depression in RA patients from low- and middle-income countries, like Ethiopia, are still scarce, despite the growing recognition of the link between RA and mental health disorders. The lack of research restricts the development of culturally relevant interventions to address the mental health needs of RA patients in these regions and makes it more difficult for us to understand the unique challenges these patients face.

As a result, there is a pressing need for research into the prevalence of anxiety and depression among RA patients in Ethiopia, as well as the factors that contribute to these mental health conditions. This data will be critical in developing targeted interventions and improving the mental health outcomes of RA patients in this region.

1.3 Significance of the study

This study is significant because it fills a critical knowledge gap in the understanding of mental health among RA patients in Ethiopia. By looking into the prevalence and risk factors for anxiety and depression in this population, the study can help develop targeted interventions to improve mental health outcomes. Furthermore, the findings may help to raise awareness about RA patients' mental health needs and advocate for improved access to mental health services in the region. Finally, this study has the potential to improve the overall health and quality of life for RA patients in Ethiopia.

2. Literature Review

A systematic review of 72 studies was conducted, with 13 189 patients included. There were 43 different methods for defining depression reported. Meta-analyses revealed that the prevalence of major depressive disorder was 16.8% (95% CI 10%, 24%). According to the PHQ-9, the prevalence of depression was 38.8% (95% CI 34%, 43%), while the HADS with thresholds of 8 and 11 showed prevalence levels of 34.2% (95% CI 25%, 44%) and 14.8% (95% CI 12%, 18%), respectively(6).

A study done on 517 participants, 17.6% had anxiety symptoms, while 27.7% had depression symptoms. The multivariable logistic regression analysis revealed that DAS28 did not have an independent association with anxiety or depression symptoms. The severity of DAS28 patient global assessment (PtGA) was linked to anxiety and depression symptoms, as were HAQ-DI scores ≤ 0.5. Patients who used steroids were more likely to experience depression than those who did not use steroids(5).

This study was conducted in Spain, and 1074 undergraduate students (71% women and 29% men) participated. The age ranged from 18 to 42, with an average of 21.73 ± 5.12 years. Of our participants, 23.6% and 34.5% reported anxiety and stress symptoms that were above the normal range, respectively(4).

A prospective observational study was conducted, in 169 RA patients, and 85 healthy controls were enrolled. Patients with RA had a higher mean depression score (19.65 ± 1.44) compared to the control group's 14.4 ± 1.31. Patients with RA had a mean anxiety score of 19.44 ± 2.4. Approximately 71% of patients with RA were diagnosed with psychiatric issues, whereas only 7.1% of those in the control group had depression or anxiety. (7).

A cross-sectional study was conducted in a total of 56 RA patients, and the results show that increased baseline depression and anxiety were associated with increased disease activity at one-year follow-up. At 12-month follow-up, there was a significant relationship between depression and anxiety and the subjective components of the DAS28: tender joint count and patient global assessment. After controlling for age, gender, disease duration, and baseline tender joint count and patient global assessment, higher levels of depression and anxiety at baseline were linked to higher tender joint count and patient global assessment scores at 1-year follow-up(8).

A secondary analysis of the clinical trial was performed on 379 patients, and baseline depression/anxiety symptoms were associated with improved DAS-28 outcomes and tender joint counts. Persistent depression/anxiety symptoms were linked to higher DAS-28 scores, HAQ scores, tender joint counts, functional disability and patient global assessments of disease activity(9).

A study was conducted to assess the relationship between clinical remission in RA and patient-reported outcomes (PROs), and the findings revealed that patients who achieved clinical remission were less likely to maintain symptoms of depression or anxiety than non-remitters. Fatigue and pain had a significant impact on changes in depression status, but not on anxiety status. Finally, clinical remission was significantly linked to improvements in all PRO measures(10).

In a study of 265,413 patients, baseline anxiety and coping with pain were associated with DAS at 3 months; coping with pain at 6 months was associated with DAS at 9 months; and fatigue at 12 months with DAS at 15 months. Psychosocial factors exhibited moderate correlation. The effects on DAS were primarily due to tender joint count and global health(11).

A systematic review was done. Anxiety prevalence ranged from 2.4% to 77% across 47 studies, and was primarily determined using standardized self-report measures, with the Hospital Anxiety and Depression Scale being the most commonly used; only eight studies used a clinical diagnostic interview to confirm a specific anxiety diagnosis. Physical disability, pain, disease activity, depression, and quality of life were all significant predictors of anxiety in RA(12).

In the cross-sectional study, 414 RA patients were recruited prospectively. RA activity was measured using the Disease Activity Score, and patients' disability was assessed using the Health Assessment Questionnaire. Pain perception levels were stratified using the Visual Analog Scale. Depression was prevalent in 63.6% of RA patients, as was anxiety in 84.1%. Mixed anxiety and depression were found in 60.2% of the study participants(13).

Four hundred and sixty-four patients participated in a cross-sectional study. The mean age was 59 years, the median disease duration was 9.9 years, and 85% of patients were female. According to the Thai HADS cutoff value of eight or higher, 12.5% and 14.5% of patients had some level of depression and anxiety, respectively(14).

3. Objective

3.1. General Objective

- To determine the prevalence of anxiety and depression and their associated factors among RA patients attending selected hospitals in Addis Ababa, Ethiopia.

3.2. Specific Objectives

- To assess the prevalence and severity of depression and anxiety in patients with RA.
- To identify factors associated with depression and anxiety among RA patients.

4. Methods

4.1 Study area

The study was conducted at TASH, rheum rheumatology, internal medicine specialty clinic, and Lancet General Hospital located in Addis Ababa, the capital city of Ethiopia which is located in the central part of Ethiopia. Tikur Anbessa Specialized Hospital is Ethiopia's largest referral hospital and the primary teaching hospital for Addis Ababa University's School of Medicine. It was founded in 1964 and has since played a critical role in providing comprehensive healthcare services to Ethiopians. Tikur Anbessa Specialized Hospital is the largest referral hospital in the country, with 700 beds, 200 doctors, 379 nurses, and 115 other health professionals dedicated to providing health care services. Rheumatology and internal medicine specialty clinics and Lancet General Hospital are known private health institutions that provide comprehensive health care services to Ethiopians.

4.2 Study design

Institutional-based multicenter cross-sectional study

4.3 Sampling technique

A consecutive sampling method was used. All patients who visited the rheumatology outpatient departments (OPDs) during the study period were assessed for eligibility. After obtaining verbal informed consent, the patients were interviewed using prepared tools.

4.4. Population

4.4.2Source population

5. All RA patients visited TASH, Rheum Rheumatology and Internal Medicine Specialty Center, and Lancet General Hospital

4.4.3 Study population

6. All adult RA patients volunteer to participate in the study at TASH, Rheu Rheumatology and Internal Medicine Specialty Center, and Lancet General Hospital

4.5. Eligibility criteria

4.5.1. Inclusion criteria

- Patients diagnosed with RA using the 2010 ACR/EULAR classification criteria;
- Patients aged 20 or older;
- Patients gave written informed consent to participate in the study.

4.5.2. Exclusion criteria

1. Patients with psychiatric disorders (e.g. bipolar disorder, schizophrenia).
2. Patients had outpatient appointments in the psychiatry or psychosomatic medicine departments.
3. Patients who did not fill out the PHQ9, GAD7, HAQ-DI and MMAS4 questionnaire

4.5. Sample size determination

To determine the sample size, a single population proportion formula is used. For the sample size for the descriptive cross-sectional study, we used the expected prevalence to be 50% since there was no study done in Ethiopian referral hospitals.

$$n = \frac{(Z\alpha/2)^2 * P * (1-P)}{d^2}$$

Where: n = sample size

Zα/2 = the standard normal deviate (set at 1.96 for a 95% level of precision)

P = the expected prevalence (set at 50% for this example)

d = the acceptable margin of error (set at 4% for this example)

Therefore, the sample size would be: n = (1.96^2 * 0.5 * (1–0.5)) / 0.04^2 = 384

Since the sample frame is less than 10000, we use the adjustment formula, nadj. = n/ ((1+ (n/N)). Where nadj. = Adjusted sample size, n = calculated sample size, n = 384 and N = study population, N=**1000**, nadj. = 384/ (1+(384/1000) ≈**277**, Considering a 10 % non-response rate

The sample size will be **308.**

4.6 Study variable

4.6.1 Dependent variable

Levels of anxiety and depression symptoms in patients with RA

4.6.2 Independent variable

Socio-demographic characteristics

- ✓ age
- ✓ sex

Factors related to anxiety and depression characteristics

- ✓ Disease Activity
- ✓ Pain Severity
- ✓ Physical Disability:
- ✓ Patient Global Assessment

- ✓ Medication Use

4.7 Operational definition

Depression /anxiety assessment-PHQ-9/GAD-7 score

- **PHQ-9**–0 up to 4-no depression,5-9 mild depression,10-14 moderate depression,15-19-moderately severe depression,20-27-severe depression.
- **GAD-7-NO anxiety**-0-4, Mild anxiety disorder-5-9, moderate-10-14 ,above 15-severe.
- **RA Disease Activity:** DAS-28-score(using crp as inflammatory marker)

  DAS-28-<2.6–remission, 2.6-≤3.2-low disease activity

  >3.2-≤5.1-moderate disease activity, >5.1-high disease activity

- **Quality of life: HAQ-D1:**0 to 1-mild to moderate difficulty,1 to 2-moderate to severe difficulty,2 to 3 severe to very severe difficulty
- Patient Global Assessment (PtGA): A subjective measure of the patient's overall health status.

  PGA- ≤2-low disease activity,>2-High disease activity

- **Medication Use**: MMAS-4 scales, specifically the use of disease-modifying anti-rheumatic drugs (DMARDs) and steroids.

  0-higher adherence, 2 or 3-moderate adherence, 4-higher adherence

4.8 Data collection tool and procedure

This study aims to assess factors associated with anxiety and depression in RA patients attending follow-ups at Black Lion Specialized Hospital, Rheum Rheumatology and Internal Medicine Specialty Center, and Lancet General Hospital, Addis Ababa Ethiopia. Data was collected by using a structured questionnaire inserted into the Kobo toolbox. This method allows for efficient and accurate data collection reduces error and increases the overall reliability of the collected data.

4.8.1 Data quality control

The checklist was pretested on 15 (5% of the charts) randomly selected patients to maintain data quality before starting the actual data collection period. Two days of training will be given to data collectors and a supervisor working outside of the study area regarding the data collection

process and tools before data collection begins. Supervisors and principal investigators monitor the data collection procedure daily for completeness and consistency of collected data.

4.8.2 Data processing and analysis

Before the analysis, data will be coded, cleaned, and checked for any missing value. Data was entered into SPSS version 26 software. The descriptive data was described using mean with standard deviation, median with interquartile range, and mode. The overall factors associated with anxiety and depression in RA patients was assessed retrospectively by using adopted questionnaires. The odds ratio with a 95% confidence interval was used to determine the strength of association between dependent and independent variables. The model fitness test was performed using the Hosmer-Lemeshow test.

A P-value less than 0.05 were considered statistically significant. Variables with a p-value of less than 0.25 were included in the bi-variable analysis. Multivariable logistic regression analysis was carried out to identify factors associated with anxiety and depression in RA patients when the p-value is less than 0.05. Results are then presented using frequency tables, figures, and summary measures.

4.9 Ethical consideration

A formal letter was taken from Addis Ababa University College of Health Sciences, Department of Internal Medicine to get approval to conduct this study. The study was conducted after ethical clearance was obtained from the Ethical Institutional Review Board (IRB). Then, data was collected after getting an official letter of permission.

4.10 Dissemination of result

The plan for dissemination of the results would involve several strategies to ensure that the findings are widely disseminated to relevant stakeholders. These stakeholders may include the intensive unit department, emergency department, residents, nurses, and the hospital administration. Some of the key ways to disseminate include conferences and presentations, Publications in peer-reviewed journals, Hospital meetings and morning presentations and social media.

5. Results

5.1 Socio-demographic characteristics of the respondents

A total of 291 RA patients were included in the study, resulting in a response rate of 94.4%. The majority were female (251; 86.3%), with a mean age of 51.18 years (±13.05 SD). Most respondents were aged between 36–50 years (43.3%) or above 50 years (48.1%). The majority of participants were recruited from Tikur Anbessa Specialized Hospital (see Table 1).

Table 1: Socio-demographic characteristics of RA patients in Addis Ababa, Ethiopia (n=291).

Variables		**Frequency (n)**	**Percentage (%)**
Age (years)	21-35	25	8.6
	36-50	126	43.3
	≥50	140	48.1
Sex	Male	40	13.7
	Female	251	86.3
Study site	Rheum rheumatology and internal medicine specialty clinic	50	17.2
	Lancet General Hospital	62	21.3
	TASH	179	61.5

5.2 Characteristics of patients with RA

The study revealed the mean DAS28 score was 2.76± 0. 984 (SD). The majority of RA patients were found to be in clinical remission based on the DAS28 score (50.5%). On the other hand, the mean HAQ-DI score was 0.8801 ± 0.669 (SD) with about two-thirds (63.9%) having mild to moderate difficulty. However, based on the patient global assessment (PGA), 70.8% reported high disease activity. In terms of functional status, 63.9% of patients experienced mild to moderate difficulty according to the HAQ Disability Index. Regarding treatment behavior, 69.1% of the participants demonstrated good medication adherence.

Table 2: Characteristics of patients with RA in Addis Ababa, Ethiopia (n=291)

Variables		**Frequency**	**Percentage**
DAS28 score	Clinical Remission	147	50.5
	Low Disease Activity	53	18.2

	Moderate Disease Activity	89	30.6
	High Disease Activity	2	0.7
PGA	Low Disease Activity	85	29.2
	High Disease Activity	206	70.8
HAQ Disability Index	Mild to Moderate Difficulty	186	63.9
	Moderate to Severe Difficulty	88	30.2
	Severe to Very Severe	17	5.8
Medication Adherence	Poor Adherence	32	11.0
	Moderate Adherence	58	19.9
	Good Adherence	201	69.1

5.5 Anxiety and depression among RA

Among the study participants, the overall prevalence of anxiety, as assessed by the GAD-7, was 32.4% (95% CI: 31.2%, 40.7%). Of those with anxiety, 27.3% experienced mild anxiety, and 4% had a severe anxiety disorder (Figure 1).

On the other hand, the overall prevalence of depression was also 39.9% (95% CI: 34.2%, 45.7%). Based on the PHQ-9 cutoff values, 25.4% of participants had mild depression, while 2.1% had severe depression (Figure 1).

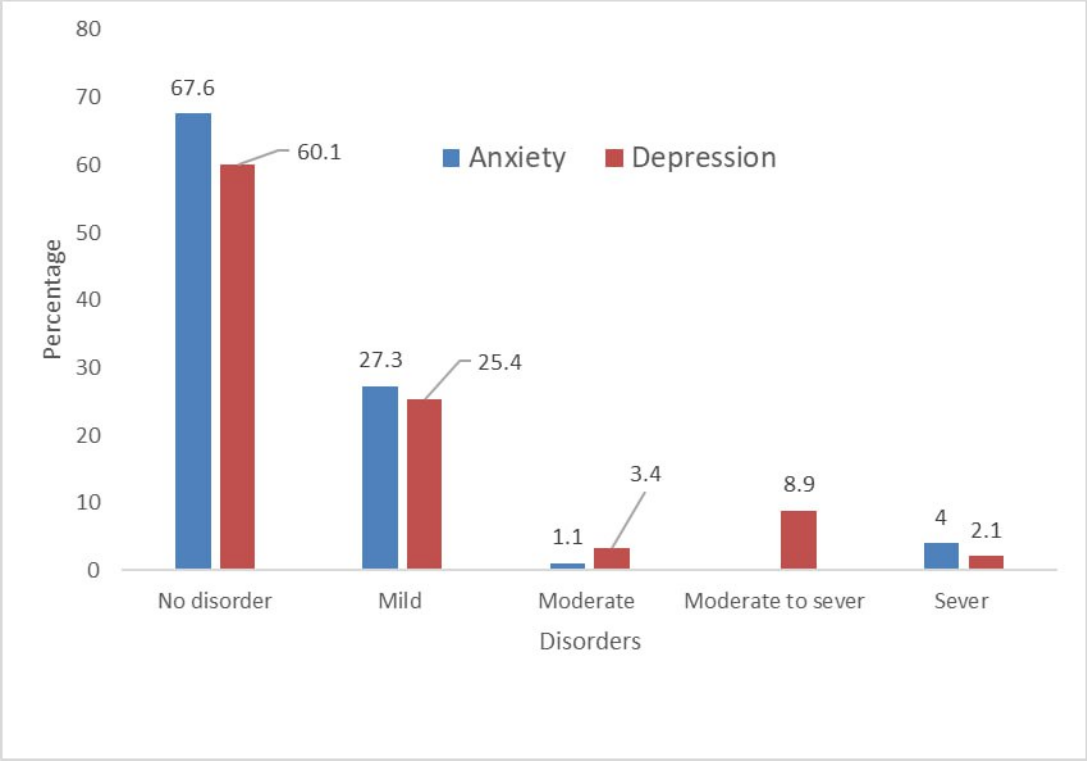

Figure 1: Depression and anxiety disorders among RA in Addis Ababa, Ethiopia (n=291).

5.6 Factors associated with depression

In the bivariate logistic regression analysis, the following variables had p-values below 0.25 for inclusion in the multivariable model: age above 50 years (p = 0.022), female gender (p = 0.002), absence of clinical remission based on DAS28 (p = 0.000), poor medication adherence (p = 0.000), moderate to severe disability (p = 0.000) and severe to very severe disability (p = 0.000) on the HAQ-DI, and high disease activity as assessed by the patient global assessment (p = 0.000).

In the multivariable logistic regression analysis, several factors were found to significantly influence the likelihood of depression in patients with RA. Female patients had more than five times the odds of experiencing depression compared to male patients (AOR = 5.13, 95% CI: 1.87–14.0, p = 0.001). Additionally, patients who had poor adherence were over six times more likely to be depressed than those with good adherence (AOR = 6.59, 95% CI: 2.35–18.4, p = 0.000). Patients reporting moderate to severe disability were nearly four times more likely to be depressed than those with mild to moderate disability (AOR = 3.96, 95% CI: 2.15–7.31, p = 0.000), while those with severe to very severe disability had over six times the odds of

depression (AOR = 6.66, 95% CI: 1.82–24.3, p = 0.004). Lastly, high disease activity was linked to a 3.26-fold increase in the odds of depression (AOR = 3.26, 95% CI: 1.60–6.63, p = 0.001).

Table 3: Factors associated with depression in patients with RA in Addis Ababa, Ethiopia (n=291).

Variable	**COR (95%CI)**	**p-value**	**AOR (95% CI)**	P-value
Age of participants				
21-35 years	1		1	
36-50 years	0.95 (0.36, 2.47)	0.917	0.40(0.14, 1.17)	0.095
Above 50 years	2.96 (1.16, 7.55)	0.022	1.22(0.44, 3.42)	0.694
Gender of participants				
Female	3.75(1.60, 8.79)	0.002	5.13(1.87, 14.0)	**0.001**
Male	1		1	
DAS28 CRP				
Has clinical remission	1		1	
Has no clinical remission	2.64 (1.62, 4.29)	0.000	1.38(0.76, 2.51)	0.280
Medication adherence				
Poor Adherence	4.57 (2.01,10.42	0.000	6.59(2.35, 18.4)	**0.000**
Moderate adherence	1.01 (0.55, 1.86	0.957	1.22(0.60, 2.49)	0.572
Good Adherence	1		1	
HAQ-DI				
Mild to moderate difficulty	1		1	
Moderate to severe difficulty	4.79 (2.78, 8.24)	0.000	3.96(2.15, 7.31)	**0.000**
Severe to very severe	9.34 (2.90, 30.0)	0.000	6.66(1.82, 24.3)	**0.004**
Patient Global Assessment				
Low disease activity	1		1	
High disease activity	4.97 (2.63, 9.38)	0.000	3.26(1.60, 6.63)	**0.001**

5.7 Factors associated with anxiety

Bivariate logistic regression analysis was used to assess the association between each independent variable and anxiety among patients with RA. A p-value threshold of <0.25 was applied to identify candidate variables for inclusion in the multivariable logistic regression model. Based on this criterion, the following variables were selected for multivariable analysis: age above 50 years (p = 0.01), female gender (p = 0.001), absence of clinical remission based on DAS28-CRP (p = 0.001), poor medication adherence (p = 0.001), higher disability scores on HAQ-DI—specifically, moderate to severe difficulty (p = 0.001) and severe to very severe difficulty (p = 0.001)—as well as high patient global assessment (PtGA) of disease activity (p = 0.001).

The results of the multivariable analysis revealed several factors significantly associated with increased anxiety in patients with RA Female patients about five times as likely to experience anxiety compared to male patients (AOR = 4.9, 95% CI:(1.33,11.0), p = 0.001). Poor medication adherence is strongly associated with anxiety, as patients with poor adherence have more than five times the odds of experiencing anxiety compared to those with good adherence (AOR = 5.33, 95% CI (2.35, 17.4), p = 0.001). Higher disability levels, particularly moderate to severe (AOR = 2.66, 95% CI (1.15, 6.31), p < 0.001) and severe to very severe (AOR = 4.44, 95% CI: (1.72, 14.1), p = 0.004) difficulty on the HAQ-DI, are also associated with significantly higher odds of anxiety. Additionally, patients with high global disease activity, as assessed by the patient global assessment (AOR = 3.11, 95% CI:(1.44, 4.53),p < 0.001), are more than three times as likely to report anxiety compared to those with low disease activity.

Table 4: Factors associated with anxiety in patients with RA in Addis Ababa, Ethiopia (n=291).

Variable	**COR (95%CI)**	**P-value**	**AOR (95% CI)**	P-value
Age of participants				
21-35 years	1		1	
36-50 years	0.45 (0.36, 2.47)	0.81	0.33(0.11, 1.17)	0.07
Above 50 years	2.23 (1.16, 6.55)	0.01	1.9(0.44, 3.42)	0.55
Gender of participants				
Female	2.94(1.55, 6.59)	0.001	4.9(1.33,11.0)	**0.001**
Male	1		1	
DAS28 CRP Clinical remission				
Has Clinical remission	1		1	

No Clinical remission	2.33 (1.42, 3.29)	0.001	1.28 (0.56, 2.41)	0.14
Medication adherence				
Poor adherence	4.57 (2.01,10.42)	0.001	5.33(2.35, 17.4)	**0.001**
Moderate adherence	0.93 (0.52, 1.56)	0.88	1.11(0.50,1.29)	0.44
Good adherence	1		1	
HAQ-DI				
Mild to moderate difficulty	1		1	
Moderate to severe difficulty	3.33 (1.68, 6.11)	0.001	2.66(1.15, 6.31)	**<0.001**
Severe to very severe	7.22 (2.17, 26.0)	0.001	4.44(1.72, 14.1)	**0.003**
Patient Global Assessment				
Low disease activity	1		1	
High disease activity	3.82 (1.63, 7.48)	0.001	3.11(1.44, 4.53)	**<0.001**

6. Discussion

This study assessed the prevalence and predictors of anxiety and depression among RA patients in Addis Ababa, Ethiopia. The prevalence of anxiety was 32.4%, with 27.3% experiencing mild anxiety and 4% having severe anxiety. Similarly, the prevalence of depression was also 39.9%, with 25.4% having mild depression and 2.1% experiencing severe depression. Significant factors associated with both anxiety and depression included female gender, poor medication adherence, moderate to severe disability, severe disability, and high disease activity.

The study found that 39.9% of RA patients had depression, with varying severity, including 25.4% mild, 3.4% moderate, 8.9% moderate severe, and 2.1% severe depression. This prevalence is similar to the 38.8% observed at King's College Hospital in London (6). However, it is higher than rates reported in other studies, such as the 7.1% in a prospective observational study (7), 12.5% at Mahidol University in Bangkok (14), and 27.7% in Japan (5). Conversely, it is lower than a study in Iran, which reported a depression rate of 60.2% (13). The variation in depression prevalence across these studies may be explained by differences in healthcare systems, cultural attitudes, coping mechanisms, healthcare access, mental health awareness, and study design. These local factors likely influence both the prevalence and reporting of depression in RA patients.

The study found that 32.4% of RA patients experienced anxiety, with 27.3% having mild anxiety, 1.1% moderate anxiety, and 4% severe anxiety. This prevalence is lower than studies in Iran (63.6%) (13) and Spain (84.1%) (4), where higher rates of anxiety were observed. The difference may be due to variations in the cutoff points for diagnosing anxiety; our study used a HADS cutoff of 8, while other studies may have used different thresholds. Additionally, the Spanish study focused on male participants, which could explain the higher rates. In contrast, our findings were higher than those in Japan (17.6%) (5) and Mahidol University, Bangkok (14.5%) (14), where lower rates were reported, potentially due to differences in sample size, as larger samples often yield lower prevalence estimates. Cultural and socioeconomic factors, along with study design differences, may also explain these discrepancies. Despite these variations, our results were consistent with those from Spain, which reported anxiety rates of 23.6% in female participants (4) and 34.5% in male participants (4). These differences can likely be attributed to variations in cutoff points, gender distribution, sample size, and cultural factors.

Our findings indicate that the factors influencing both depression and anxiety in rheumatoid arthritis (RA) patients are strikingly similar, underscoring shared biological, psychological, and social pathways underlying these comorbid mental health conditions. Women with RA exhibited a disproportionately higher risk of anxiety and depression compared to men, as highlighted in a Thai study (14) where 85% of participants were female. This aligns with global epidemiological trends, where women are more likely to experience RA and comorbid mental health conditions. Sociocultural factors (*e.g.*, caregiving responsibilities) and biological mechanisms (*e.g.*, hormonal fluctuations) may exacerbate psychological distress in women (14). None of the reviewed studies directly evaluated the association between medication adherence and depression among patients with rheumatoid arthritis (RA). Uncontrolled disease activity resulting from poor adherence may exacerbate symptoms of depression and anxiety. Conversely, severe disease manifestations and associated psychological burdens may negatively impact medication adherence. This bidirectional relationship highlights the importance of integrated interventions that simultaneously address this health and treatment adherence, especially in populations with a high prevalence of mental health disorders, such as RA patients (14).

Disability, measured by tools like the Health Assessment Questionnaire (HAQ), emerged as a robust predictor of anxiety and depression. A secondary analysis of a clinical trial (9) linked persistent depression/anxiety symptoms to higher HAQ scores and functional disability. Similarly, a cross-sectional study in Serbia (13) with disability strongly correlating with mental health burdens. Elevated disease activity scores (*e.g.*, DAS28) were consistently associated with anxiety and depression. A multi-country longitudinal study (11) involving 265,413 patients (specific countries not stated) found that psychosocial factors like anxiety and pain coping had lagged effects on disease activity, mediated by tender joint counts and global health. Additionally, a systematic review (12) encompassing 47 international studies highlighted disease activity as a key predictor of anxiety.

7. Strengths and Limitations

This study has several notable strengths. Firstly, the multicenter design enhances the generalizability of the findings to a wider population of RA patients in Addis Ababa. Secondly, the use of standardized and validated tools such as the PHQ-9 and GAD-7 for assessing depression and anxiety, the DAS-28 for disease activity, and the HAQ-DI for disability ensures reliability and consistency in measurement. In addition, systematic data collection through digital

platforms like Kobo toolbox helped reduce data entry errors and improve overall data quality. The sample size was also adequately calculated and adjusted to account for the finite population and potential non-response, ensuring sufficient statistical power for analysis.

However, the study also has limitations. Being cross-sectional in nature, it cannot establish causal relationships between the associated factors and the presence of anxiety and depression. Additionally, the facility-based sampling limits the generalizability of the findings to those RA patients who are not attending hospital-based care. Lastly, the lack of longitudinal follow-up prevents assessment of changes in psychological outcomes over time about disease progression or treatment interventions.

7. Conclusion and Recommendations:

This study found a high prevalence of depression and anxiety among patients with RA attending public hospitals in Addis Ababa. Several factors were significantly associated with these mental health conditions, including female gender, poor medication adherence, high disease activity, and increased disability. These findings underscore the considerable psychological burden experienced by RA patients, which may negatively impact treatment adherence, disease outcomes, and quality of life.

Based on the results of this study, several key recommendations can be made to address the mental health challenges faced by RA patients. First, routine mental health screenings should be incorporated into regular clinical visits for RA patients. Tools such as the PHQ-9 and GAD-7 can be used to identify depression and anxiety early, allowing for timely intervention. Additionally, a multidisciplinary approach involving both rheumatologists and mental health professionals is recommended to ensure comprehensive care for RA patients, addressing both physical and psychological health. Improving access to mental health services is also crucial, particularly in regions with limited resources. Lastly, further research is needed to evaluate the effectiveness of integrated mental health interventions, which could help refine treatment strategies and improve patient outcomes.

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8. APPENDIX

Participants' Information Sheet

This is research on anxiety and depression in rheumatoid patients and we are collecting data for a research purpose. This form explains why we are doing this study, your role in the study, the benefits and risks of involving in this study, compensations, and confidentiality of the information you give us.

a. Purpose–The purpose of this study is to assess factors associated with depression and anxiety in RA patients who have follow-ups at Black Lion Specialized Hospital, Rheum Rheumatology and Internal Medicine Speciality Clinic, and Lancet General Hospital in Addis Ababa Ethiopia.
b. Procedures to be carried out–A brief introduction will be given by the data collector and the data collector will administer the questionnaires after interviewing consenting patients. There will not be any invasive procedures.
c. Risks associated with the study–Apart from the time you spend with us we do not see any risk that you will undergo by participating in this study.
d. Benefits of the study– this study will focus on depression and anxiety associated with RA so, if you or anyone affected by this disease were diagnosed to have depression and anxiety you will be linked to a psychiatric clinic. This also adds the advantage of the patients having the appropriate follow-up and taking their medication.
e. Compensations–There are no compensations.
f. Confidentiality of your information–The information you give during this study will be confidential. Once the data is entered into a computer, it will be coded and become unidentifiable/ anonymous. Your personal information that could lead to your identification will never be disclosed both in oral or written form.
g. Termination of the study–You will only be recruited based on your willingness and without any obligation to participate in the study. Once you get involved in the study, you have also the full right to withdraw your participation before completing the study**.**

I would also like to inform you that this study is approved by the ethical committees of the Department of Psychiatry, Addis Ababa University.

Participant consent form

Participant consent form

My name is**.** After having information about the purpose of this study I would like to ask for your consent to participate in this study entitled "Factor associated with anxiety and depression in RA pt–The validation of PHQ-9, GAD-7, HAQ-D5, MMAS-5 in black lion hospital, Rheum rheumatology and medical center and Lancet General Hospital.

Participating in this study will only depend on your decision to do so. You have all the right to withhold information, refuse, or drop out of the study any time you want to do so without needing to explain to anyone. Withdrawing from the study will have no effect on you. All the information you give during the study will be kept confidential.

You have all the right to ask and get clarification at any time. In case you have doubts or questions, you can use the above address to access the principal investigator.

I finally would like to confirm your agreement by signing your name if you agree.

Signature of patient Date

Signature of data collector Date

1. **English version questionnaire**

Section 1: Demographic Information	
1.1. Participant *ID.*:	
1.2. Age:	
1.3. Gender:	
1.4. Location	

3.1. Patient Health Questionnaire–9 (PHQ-9)

Over the past 2 weeks, how often have you been bothered by any of the following problems?

1) Little interest or pleasure in doing things?
2) Feeling down, depressed or hopeless?
3) Trouble falling or staying asleep, or sleeping too much?
4) Feeling tired or having little energy?
5) Poor appetite or over-eating?
6) Feeling bad about yourself–or that you are a failure or have let yourself or your family down?
7) Trouble concentrating on things, such as reading the newspaper or watching television?
8) Moving or speaking so slowly that other people could have noticed? Or the opposite–being so fidgety or restless that you have been moving around a lot more than usual?
9) Thought that you would be better off dead or of hurting yourself in some way?

- Not at all 0
- Several days 1
- More than half the days 2
- Nearly every day 3

If said yes to any of the problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

- Not difficult at all
- Somewhat difficult
- Very difficult
- Extremely difficult

3.2: GAD 7-ANXIETY

Over the last 2 weeks, how often have you been bothered by the following?	Not at all(5)	Several days	More than half the days	Nearly Every day
1. Feeling nervous, anxious, or on edge	23(35)			
2. Not being able to stop or control worrying				
3. Worrying too much about different things				
4. Trouble relaxing				
5. Being so restless that it is hard to sit still				
6. Becoming so easily annoyed or irritable				
7. Feeling afraid, as if something awful might happen				

Column total _____+ _____+ _____+ _____=

Total score=_____

3.3-Health Assesment Questionnaire(HAQ-DI)

Name :_____ Time:_____

Please place an ‘in the box that best describes your abilities over the past week:

	Without any difficulty	some difficulty	with much difficulty	unable to do

DRESSING & GROOMING

Are you able to:

Dress yourself including ☐ ☐ ☐ ☐

Shoelaces and buttons?

Shampoo your hair? ☐ ☐ ☐ ☐

ARISING

Are you able to:

Stand up from a straight chair? ☐ ☐ ☐ ☐

Get in and out of bed? ☐ ☐ ☐ ☐

EATING

Are you able to:

Cut your meat? ☐ ☐ ☐ ☐

Lift a full cup or glass to your mouth? ☐ ☐ ☐

Open a new milk carton? ☐ ☐ ☐ ☐

WALKINGAre you able to:

Walk outdoors on flat ground? ☐ ☐ ☐ ☐

Climb up five stairs? ☐ ☐ ☐ ☐

Please check any aids or devices that you use for any of the above activities:

☐ Devices used for dressing ☐built-up or special utensils ☐ crutches

(button hook, zipper pull, etc) ☐ cane ☐ wheelchair

☐Special or built-up chair ☐walker

Please select any categories for which you usually need help from another person:

☐ Dressing and grooming ☐ Arising ☐ Eating ☐ Waking

Please place an ‘in the box which best describes your abilities over the past week:

	Without any difficulty	some difficulty	with much difficulty	unable to do

HYGIENE

Are you able to:

Wash and dry your body? ☐ ☐ ☐ ☐

Take a tub bath? ☐ ☐ ☐ ☐

Get on and off the toilet? ☐ ☐ ☐ ☐

REACH

Are you able to:

Reach and get down a 5-pound

Object(such as a bag of sugar) ☐ ☐ ☐ ☐

From above your head? ☐ ☐ ☐ ☐

Bend down to pick up clothing

from the floor. ☐ ☐ ☐ ☐

GRIP

Are you able to:

Open car doors? ☐ ☐ ☐ ☐

Open previously opened jars? ☐ ☐ ☐ ☐

Turn faucets on and off? ☐ ☐ ☐ ☐

ACTIVITIES

Are you able to:

Run errands and shops? ☐ ☐ ☐ ☐

Get in and out of a car? ☐ ☐ ☐ ☐

Do chores such as vacuuming or yard work? ☐ ☐ ☐ ☐

Please check any aids or devices that you usually use for the above activities:

☐ Raised toilet sits ☐ Bathtub bar ☐ Long handled appliances for reach in the bathroom

☐ Bathtub sit ☐ Long handled appliances ☐ Jar opener(for previously opened jars)

Please check any categories for which you usually need help from another person:

☐ Hygiene ☐ Reach ☐ Gripping and opening things ☐ Errands and chores

Your activities: to what extent are you able to carry out your everyday physical activities such as walking, climbing stairs, carrying groceries or moving a chair?

Completely mostly moderately a little not at all

☐ ☐ ☐ ☐ ☐

Your pain: how much pain have you had over the past week?

On a scale of 0 to 100(where 0 represents no pain and 100 represents severe pain)

Please record the number below.

☐☐☐

Your health: please rate how well are you doing on a scale of 0 to 100(where 0 represents very well and 100 represents very poor health), please record the number below

☐☐☐

3.4-Morisky medication taking adherence scale-MMAS(4 items)

Please check one box on each line

Yes No

1. Do you ever forget to take your rheumatoid ☐ ☐
arthritis medicine?

2. Do you ever have problems remembering to ☐ ☐
take your RA medication?

3. When you feel better do you sometimes stop
taking your RA medicine? ☐ ☐

4. Sometimes if you feel worse when you take
your RA medicine, do you stop taking it? ☐ ☐

3.6: Disease Activity Score (DAS 28)	**Yes**	**No**
Tender joints		
If yes tender joints count		
Swollen joints		
If yes swollen join count		
ESR (mm/h) or CRP (mg/l):		
How active was your RA on average during the last week from 10?		
DAS 28 score		

3.6: Patient Global Assessment (PGA)
how do you feel your arthritis is today? Rate from 0-10

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6.3	□□□□□ □□□□□ □□□ □□□ □□□ □□□ □□□□ □□ □□□□ □□□ □□□□□ □□□ □□□□□	0	1	2	3	[___]
6.4	□□□ □□□□□ □□□□ □□□ □□ □□□ □□□□□	0	1	2	3	[___]
6.5	□□□□ □□□□ □□□□□ □□□□ □□ □□ □□□□□ □□□ □□□□□□	0	1	2	3	[___]
6.6	□□□□□ □□□ □□□ □□□□ □□□□□□ □□□□ □□□□ □□□ □□□□ □□□□□□ □□□ □□□□□□	0	1	2	3	[___]
6.7	□□□□□ □□□□□ □□□ □□□□□□□ □□□□ □□□ □□□□□ □□□□ □□□□□ □□□□□□	0	1	2	3	[___]
6.8	□□□□□□ □□ □□□□ □□□ □□□□ □□□□ □□□□ □□□□ □□□□□□□□□ □□□ □□□□□□ □□□□□ □□□ □□ □□	0	1	2	3	[___]

	□□□□□ □□□ □□□□□□□ □□□ □□□□□□					

□□□ □□□ □ **GAD-7 ጭንቀት**

ባለፉት ሁለት ሳምንት ዉስጥ በሚከተለው ችግሮች ምን ያህል ግዜ ተጨንቀዋል?	አይደለም	በርካታ ቀናት	ከግማሽ ቀናት በላይ	በየቀኑ ማለት ይቻላል
1 የመረበሽ ስሜት፣የመጨነቅ ስሜት ወይም ጠርዝ ላይ መሰማት	0	1	2	3
2 ጭንቀትን ማቆም ወይም መቆጣጠር አለመቻል	0	1	2	3
3 ስለተለያዩ ነገሮች ከመጠን በላይ መጨነቅ	0	1	2	3
4 የመዝናናት ችግር	0	1	2	3
5 በጣም እረፍት ከማጣት የተነሳ ዝም ብሎ መቀመጥ ከባድ መሆን	0	1	2	3
6 በቀላሉ የሚናደድ ወይም የሚበሳጭ መሆን	0	1	2	3
7 ፍርሃት መሰማት፣አንድ አስከፊ ነገር ሊከሰት እንደሚችል ማሰብ	0	1	2	3

የአምድ ድምር ___ + ___ + ___ + ___=

ጠቅላላ ነጥብ ___

□□□ □□□□ የጤና ምዘና መጠይቅ(HAQ-DI)

ስም፤_____ ቀን፤_____

አባክዎን ባለፈው ሳምንት የእርስዎን ችሎታዎች በተሻለ ሁኔታ የሚገልጽ''x'' ሳጥን ዉስጥ ያስቀምጡ፤

ያለምንም አንዳንዴ ብዙ ጊዜ አለመቻል መቸገር መቸገር መቸገር

<u>መልበስ እና ንጽህናን መጠበቅ ትችላለህ፡</u>

ልብስ መልበስ፣የጫማ ማሰሪያዎችን እና □ □ □ □

ቁልፎችን ጨምሮ?

ጸጉርዎን በሻምፑ መታጠብ? □ □ □ □

<u>መነሳት ትችላለህ</u>

ከወንበር ላይ መነሳት? □ □ □ □

አልጋ ዉስጥ መግባትና መዉጣት? □ □ □ □

<u>መብላት ትችላለህ</u>

ለራስዎ ስጋ መቁረጥ? □ □ □ □

አንድ ሙሉ ኩባያ ወይም ብርጭቆ □ □ □ □

ወደ አፍዎ ማንሳት?

አዲስ የወተት ካርቶን መክፈት? □ □ □ □

<u>መራመድ ትችላለህ</u>

ጠፍጣፋ መሬት ላይ ከቤት ውጭ መራመድ? ☐ ☐ ☐ ☐

አምስት ደረጃዎች መውጣት? ☐ ☐ ☐ ☐

እባኮትን ከላይ ለተዘረዘሩት ተግባራት ብዙዉን ጊዜ የሚጠቀሙባቸዉን መሳሪያዎች ያረጋግጡ፤

☐ለመልበስ የሚያገለግሉ መሳሪያዎች ☐የተገነቡ ወይም ልዩ እቃዎች ☐ክራንች

☐የልብስ መቆለፊያ(የዚፕ መሳቢያ ወዘተ) ☐ሽመል(ከዘራ) ☐ተሽከርካሪ ወንበር

☐ልዩ የተገነባ ወንበር ☐ምርኩዝ(መራመጃ)

እባኮትን አብዛኛዉን ጊዜ ከሌላ ሰው እርዳታ የምትፈልግባቸዉን ምድቦች አረጋግጥ፤

☐ለመልበስ እና ንጽህና ለመጠበቅ ☐ለመነሳት ☐ለመብላት ☐ለመራመድ

ያለምንም አንዳንዴ ሁልጊዜ አለመቻል

መቸገር መቸገር መቸገር

ንጽህናህን መጠበቅ ትችላለክ

ገላዎን መታጠብ እና ማድረቅ? ☐ ☐ ☐ ☐

የመታጠቢያ ገንዳ ተጠቅሞ መታጠብ? ☐ ☐ ☐ ☐

መጸዳጃ ቤት ገብቶ መውጣት? ☐ ☐ ☐ ☐

መድረስ ትችላለክ?

ባለ 5 ፓዉንድ የሚመዝን ነገር(ስኳር ያለው እቃ) ☐ ☐ ☐ ☐

ከጭንቅላትክ በላይ ማውረድ?

ከወለሉ ላይ ልብስ ለማንሳት ጎንበስ ማለት? ☐ ☐ ☐ ☐

መያዝ ትችላለክ

የመኪና በሮች መክፈት? ☐ ☐ ☐ ☐

ቀደም ብለዉ የተከፈቱ ማሰሮዎችን ይከፍታሉ? ☐ ☐ ☐ ☐

ቧንቧዎች መክፈትና መዝጋት? ☐ ☐ ☐ ☐

ምን መስራት ትችላለክ

ገበያ መውጣት እና መግዛት ☐ ☐ ☐ ☐

መኪና ዉስጥ መግባትና መውጣት? ☐ ☐ ☐ ☐

የቤት ዉስጥ ስራዎችን መስራት? ☐ ☐ ☐ ☐

እባኮትን ከላይ ለተዘረዘሩት ተግባራት ብዙዉን ጊዜ የሚጠቀሙባቸዉን መሳሪያዎች ያረጋግጡ፤

☐ከፍያለ የሽንት ቤት መከመጫ ☐የመታጠቢያ ገንዳ ባር ☐ ረጅም እጄታ ያላቸዉ እቅዎች

☐የመታጠቢያ ገንዳ መከመጫ ☐በመታጠቢያ ቤት ዉስጥ ☐የጠርሙስ መክፈቻ

ረጅም እጄታ ያላቸዉ እቅዎች (ቀደምሲልለተከፈቱ ማሰሮዎች)

እባኮትን አብዛኛዉን ጊዜ ከሌላ ሰው እርዳታ የምትፈልግባቸዉን ምድቦች አረጋግጥ፤

☐ንጽህናን ለመጠበቅ ☐ለመድረስ ☐ነገሮችን ለመያዝ እና ለመክፈት

☐ለቤት ዉስጥ ስራዎች

የእርስዎ ተግባራት እንደ መራመድ፣ደረጃ መውጣት፣ሸቀጣ ሸቀጦችን መያዝ ወይም ወንበር ማንቀሳቀስ የመሳሰሉ የእለት ከእለት እንቅስቃሴዎችን ምን ያህል ማከናዎን ይችላሉ?

ሙሉ በሙሉ	በአብዛኛዉ	በመጠኑ	ትንሽ	አልችልም
☐	☐	☐	☐	☐

ህመምዎ፤ባለፈው ሳምንት ምን ያህል ህመም አጋጥሞታል?

ከ0እስከ100(ዜሮ ምንም ህመም የሚወክልበት እና 100 ከባድ ህመም የሚወክል ከሆነ)እባክዎ ከዚ በታች ቁጥሩን ይመዝግቡ

□□□

ጤናዎ፡እባኮትን ከ0 እስከ 100(0 በጣም ጥሩ እና 100 በጣም ከባድ ህመምን ይወክላል)

እባክዎ ከዚ በታች ቁጥሩን ይመዝግቡ

□□□

□□□ □□□□ የሞሪስኪ መድሃኒት አወሳሰድ ልኬት-MMAS (4-ነጥቦች)

<u>እባክዎ በእያንዳንዱ መስመር ላይ አንድ ሳጥን ላይ ምልክት ያድርጉ</u>

አዎ አይደለም

1 የእርስዎን የሩማቶይድ አርትራይተስ መዳሃኒት □ □

መውሰድ ይረሳሉ?

2 የእርስዎን የሩማቶይድ አርትራይተስ መድሃኒት

ለመውሰድ ማስታወስ ላይ ችግር አጋጥሞት ያውቃል? □ □

3 ጥሩ ስሜት ሲሰማዎት አንዳንድ ጊዜ የሩማቶይድ

አርትራይተስ መድሃኒቶን መውሰድ ያቆማሉ? □ □