Original

The Depression Prevalence in Chinese Patients with Rheumatoid Arthritis: A Systematic Review and Meta-analysis

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Abstract

Background: The chronic course and recurring acute episodes of rheumatoid arthritis (RA) can significantly affect the psychological and mental health of patients. This study aimed to investigate the prevalence of depression in Chinese patients with rheumatoid arthritis (RA) through a systematic review and meta-analysis.

Methods: We conducted a comprehensive literature search on electronic databases from the inception of the database to April 2023. The inclusion criteria included cross-sectional or case-control studies on depression prevalence with a sample size of at least 50 participants. The data was extracted from the included studies and analyzed to calculate the pooled depression prevalence, along with a 95% confidence interval (CI), using Review Manager 5.3 software (Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014).

Results: Thirteen studies (n = 29,113) were included, with females accounting for over 50% of all participants. Based on the data pooled from all 13 studies, the observed depression prevalence in Chinese individuals with RA was 37% (95% CI: 28–46%; $I^2 = 95\%$; $p < 0.0001$). A subsequent subgroup analysis was conducted on scale types, age, and gender. Regarding scale types, the depression prevalence was assessed using various scales included the Hospital Anxiety and Depression Scale (HAMD), Hamilton Depression Scale (HADS), Center for Epidemiologic Studies Depression (CES-D) scale, Diagnostic and Statistical Manual of Mental Disorder (fourth edition DSM.IV) diagnostic criteria, and Self-rating Depression Scale (SDS) were 50%, 35%, 58%, 39%, and 41%, respectively. Based on mean age, five studies researched RA individuals <50 years old, establishing a depression prevalence of 48% (95% CI: 32–65%). In contrast, eight studies researched RA individuals ≥50 years old, establishing a depression prevalence of 41% (95% CI: 32–51%). Gender-based analysis indicated a depression prevalence in female RA individuals of 45% (95% CI: 37–55%) and 39% (95% CI: 29–48%) among male RA patients. Depression prevalence established significant correlations with specific scales, including the HAMD scale (odds ratio (OR) 4.93, 95% CI: 1.79–10.2), CES-D scale (OR 2.83, 95% CI: 1.71–4.65), DSM.IV criteria (OR 0.75, 95% CI: 0.38–1.51), and SDS (OR 0.95, 95% CI: 0.32–2.16). Additionally, depression prevalence was associated with age categories (age ≥50: OR 1.25, 95% CI: 0.59–2.70; age <50: OR 1.99, 95% CI: 0.93–3.81), as well as gender (female: OR 1.63, 95% CI: 0.64–4.57; male: OR 1.07, 95% CI: 0.38–3.03), although some associations did not reach statistical significance.

Conclusion: The depression prevalence was high in Chinese individuals with RA, especially in females and patients under 50 years old. These findings suggest the need for improving detection and management of depression in RA patients.

Keywords

rheumatoid arthritis; depression; common mental disorders; prevalence; meta analysis

Introduction

Depression can manifest as a loss of interest or pleasure in daily life, often accompanied by symptoms like insomnia or drowsiness, changes in appetite or weight, and lack of concentration [1,2]. An international epidemiological survey reported a 3% depression prevalence in the

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Japanese population. Comparatively, the United States exhibited a higher prevalence rate, establishing a 16.9% depression prevalence [3]. Furthermore, a recent global meta-analysis targeting older adults demonstrated a depression incidence rate of 28.4%, suggesting a considerable prevalence of depression among older adults globally [4]. In addition to older adults, the significant prevalence of depression also extends to other demographic groups, including Chinese students and adolescents [5,6]. Large-scale data from China indicates that depression is a noteworthy mental disorder among college students and adolescents [7]. The high prevalence among various populations highlights the importance of addressing mental health concerns across various age groups and nationalities.

Inflammation results from long-term physiological stimulation of the innate immune system [8]. Rheumatoid arthritis (RA) is a common autoimmune disease characterized by erosive arthritis [8]. According to the 2010 Disease Burden Study, the estimated global prevalence of RA is 0.24% [9], with the incidence and prevalence rates in females being twice that of males [10]. The chronic and recurring nature of RA can significantly impact the psychological and mental health of patients [11]. Depression is commonly observed in RA patients, often attributed to factors such as disability or concerns about disability, financial burdens, and drug side effects, which affects the therapeutic effect and aggravates the clinical manifestations of RA. Compared to the general population, studies indicate a high prevalence of depression in individuals with RA [12]. Recent research shows that about 66% of RA patients experience depression, while 70% of patients exhibit anxiety symptoms. The co-occurrence of depression in RA individuals is significantly associated with increased pain and fatigue, decreased quality of life, increased number of complications, and even elevated mortality rates [11]. The relationship between depression and rheumatoid arthritis is bidirectional, with data demonstrating that individuals with RA have a 47% higher risk of depression compared to those without RA, while depressed individuals have a 34% higher risk of RA [13]. Non-inflammatory pain associated with depression contributes to the overall pain scores in RA patients [14]. Enhancing the management of physical health conditions may be an important aspect in improving subjective health and quality of life for individuals with depression [15].

There are significant differences in reported depression rates among individuals with RA, with prevalence ranging from 9.5% to 41.5%. These discrepancies can be attributed to various factors, including differences in study design, population characteristics, and diagnostic criteria for both depression and the RA study population [16]. Due to the wide range of prevalence rates, it is difficult to determine the potential impact and disease burden of depression in RA patients. Consequently, this study aims to investigate the pooled prevalence of depression in Chinese individuals with RA, summarize the definition and standards of depression in this population, and clarify the influence of different study characteristics on depression prevalence.

Methods

Literature Search

This meta-analysis was carried out in accordance with MOOSE as shown in **Supplementary File 1**. A meta-analysis scheme and data extraction table were developed for this study. A comprehensive literature search was conducted on PubMed, Embase, CNKI, and PsycINFO databases, covering publications from the inception of database to April 2023. The collected publications included cross-sectional studies or case–control studies. The search terms included “rheumatoid arthritis”, “RA”, “depression”, “depression disorder”, and “depression symptom”. Additionally, the references of all full-text papers were examined to ensure the inclusion of relevant literature meeting the specified criteria.

The Inclusion and Exclusion Criteria

The inclusion criteria of this study included: (1) The study population should consist of Chinese individuals aged 18 and older; (2) A clear diagnosis of rheumatoid arthritis (RA) based on clinical symptoms, physical examination, laboratory tests, and imaging examinations; (3) The selected studies must provide a clear definition or standard for diagnosing depression [17]; (4) The selected studies must use a cross-sectional or case–control study design; (5) The inclusion of participants should not exhibit significant selection bias; (6) Sample size $\geq$50. The exclusion criteria included: (1) Studies that provide only abstracts without access to full-text articles; (2) Studies with incomplete data; (3) Literature that has undergone repeat screening; (4) Literature with incomplete data extraction.

Data Extraction, Quality Evaluation, and Publication Bias

The final inclusion of literature was determined by two independent researchers. The following data were extracted from the included studies: the first author, year of publication, sample size, number of individuals with depression, literature source, average age, diagnostic criteria, de-

pression evaluation scale, and gender distribution. Two independent researchers cross-verified the accuracy and authenticity of the data. The quality of the included studies was assessed using the Newcastle Ottawa Scale (NOS), with a maximum score of 13, where higher scores indicated higher research quality [18]. In cases of inconsistency between data extraction and quality evaluation, articles were subjected to re-review, and discrepancies were resolved through negotiation with a third researcher. The potential publication bias was evaluated using the Begg's test and the Egger's test.

Observation Measures

Depression is commonly measured in academic literature using various validated scales. The Hospital Anxiety and Depression Scale (HADS) is commonly used in non-psychiatric hospital settings to assess the severity of anxiety and depression symptoms based on 14 items divided into two subscales. In contrast, The Hamilton Depression Scale (HAMD) is a clinician-administered questionnaire that evaluates various aspects of depression with 17 items. The Center for Epidemiologic Studies Depression (CES-D) is a self-report questionnaire widely used among the general population to measure depressive symptoms, consisting of 20 items that assess various domains related to depression. In addition, the DSM.IV provides standardized criteria for diagnosing different types and severity levels of depression based on clinical presentation and symptomatology. Lastly, the Self-rating Depression Scale (SDS) evaluates functional impairment associated with psychiatric disorders, including depression, across three domains. The utilization of these scales in the literature allows for a comprehensive assessment and characterization of depression in different contexts, enabling a more standardized and comparable evaluation of symptoms and their impact on individuals' lives.

Statistical Analysis

The number and proportion of individuals with depressive symptoms were aggregated from each study to obtain the collective prevalence rate across all studies. Statistical analysis and forest map production were completed using Review Manager 5.3 (version 5.3, Cochrane, London, United Kingdom). Statistical heterogeneity was assessed using the I^2 test of Q-statistics, with I^2 indicators ranging from 0% to 100%. In this study, $I^2 \geq 50\%$ indicated heterogeneity among the studies involving various individuals with RA, and a random-effects model was used. Subgroup analyses in RA individuals were conducted based on different types, age groups, and genders of the evaluation scale. The significance level was set at $\alpha < 0.05$.

Results

The Flowchart of the Study

Based on the predetermined retrieval strategy, a total of 3263 citations were generated, including 3255 citations from database searches and 8 citations from other sources (Fig. 1). Among these, 646 duplicate citations were identified, resulting in 2617 unique citations. Following the application of exclusion criteria, which involved eliminating non-cross-sectional studies, studies involving non-RA individuals, those with unqualified measurements of depression symptoms, and studies lacking full-text availability (n = 2560), 57 articles were read in full. Further exclusions were made for studies limited to abstracts or comments, those restricted by gender or age range, and those with incomplete data (n = 44), leaving a total of 13 studies included in the analysis.

The Quality Evaluation, Publication Bias, and Clinical Characteristics of the Included Studies

Table 1 (Ref. [19–31]) displays that all included studies were published after 2010. The study quality was evaluated using the NOS scale, indicating that the included literature was generally well-designed and of high quality. Specifically, four studies received a NOS score of 7, six studies scored 6, two studies scored 5, and one study scored 4. Among the thirteen studies, one study focused on outpatient individuals, five on inpatient settings (one was a multicenter inpatient), and seven on a combination of outpatient and inpatient individuals. The publication bias was evaluated by Begg's test ($p = 0.130$) and Egger's test ($p = 0.089$), indicating no significant publication bias. The mean age of the included subjects ranged from 44.5 to 62.1 years old, and the proportion of females in the studies consistently exceeded 50%, ranging from 71.8% to 100.0%.

The Pooled Depression Prevalence in RA Individuals

This study included a total of 13 studies involving 29,113 individuals with RA. Fig. 2 illustrates a summary of the data from these studies, revealing an overall depression incidence rate of 37% (95% CI: 28–46%; $I^2 = 95\%$; $p < 0.0001$). Among the 13 included articles, 10 were published in English, and the depression incidence rate in RA individuals from these 10 articles was 38% (95% CI: 26–49%; $I^2 = 96\%$; $p < 0.0001$, Fig. 3).

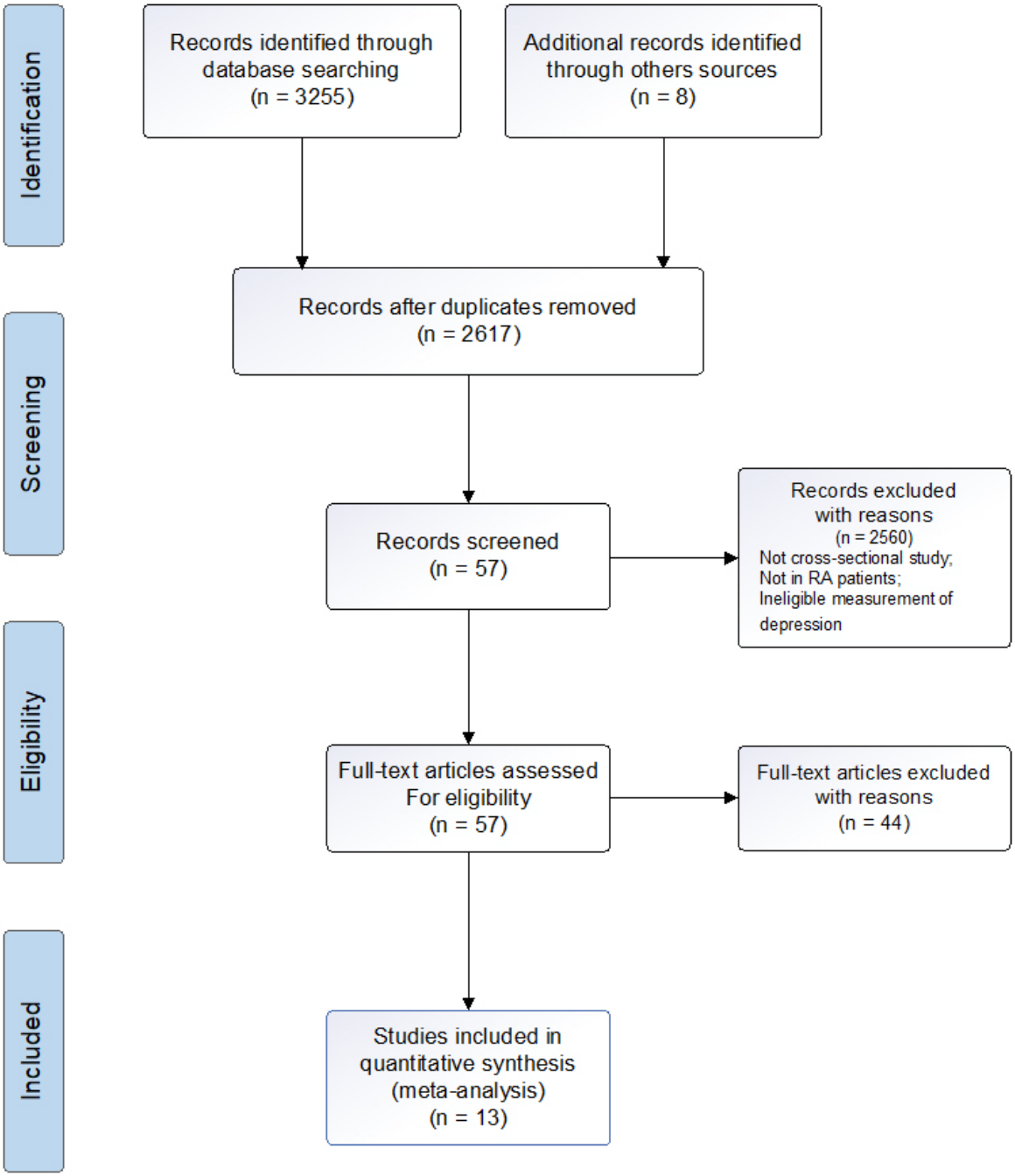

Fig. 1. The flowchart of the literature selection process. RA, rheumatoid arthritis.

The Subgroup Analysis Based on Scale Type and Age

Table 2 presents the subgroup analysis of depression prevalence based on scale type and age. The diagnostic criteria include HAMD, HADS, CES-D, DSM, and SDS. Within the HAMD scale category, three studies with a total sample size of 436 yielded an aggregated depression incidence of 50% (95% CI: 37–64%). The HADS scale was used in seven studies, totaling a sample size of 27,983 and revealing a depression incidence of 35% (95% CI: 29–46%). A single study used the CES-D scale (n = 297), reporting a depression incidence of 58% (95% CI: 53–64%). One study used DSM.IV diagnostic criteria (n = 200), establishing a depression incidence of 39% (95% CI: 32–46%). Lastly, one study used the SDS (n = 197), establishing a depression incidence of 41% (95% CI: 34–48%).

Table 1. The quality evaluation and clinical characteristics of the included studies.

First author	Published year	Published language	Study quality*	Source of study population	Mean age	The proportion of female, %	Sample size	BMI, kg/m^2	Duration of disease, years	Number of depression patients
Li [19]	2022	English	6	Outpatient or inpatient	553 ± 6.7	90.2	215	22.4 ± 3.4	10.3 ± 5.5	105
Ng [20]	2020	English	7	Inpatient	62.1 (13.5)	78.2	625	NA	NA	38
Ru [21]	2019	English	6	Outpatient or inpatient	47.6 ± 15.2	71.8	195	NA	NA	52
Geng [22]	2022	English	7	Inpatient	48.5 ± 14.1	78.9	201	NA	11.0 ± 6.8	38
Ren [23]	2023	English	6	Outpatient or inpatient	48.9 (16.9)	57.05	25,990	31.0 (8.4)	NA	2327
Liu [24]	2017	English	4	Multi-center inpatient	58.6 ± 13.5	77.4	297	NA	NA	173
Liu [25]	2019	Chinese	5	Outpatient or inpatient	50.2 ± 6.9	100	184	NA	NA	57
Lok [26]	2010	English	5	Outpatient	51.6 ± 11.2	79.0	200	NA	4 (IQR: 2–9)	78
Pu [27]	2018	English	6	Outpatient or inpatient	47.4 ± 12.9	76.4	161	23.5 ± 5.8	6.6 ± 7.0	102
Li [28]	2019	English	7	Inpatient	44.5 ± 10.6	73.3	60	20.9 ± 2.6	NA	22
Wang [29]	2021	Chinese	7	Outpatient or inpatient	47.3 ± 11.8	80.2	197	NA	5.0 ± 2.2	81
Zhang [30]	2017	English	6	Outpatient or inpatient	54.2 ± 14.9	83.8	160	22.0 ± 3.4	7.2 ± 8.2	44
Zhang [31]	2021	Chinese	6	Inpatient	56.8 ± 12.6	78.5	628	NA	6.9 ± 8.5	229

*The Newcastle Ottawa Scale (NOS) was used to evaluate the quality of the study.

NA, not available; BMI, Body Mass Index.

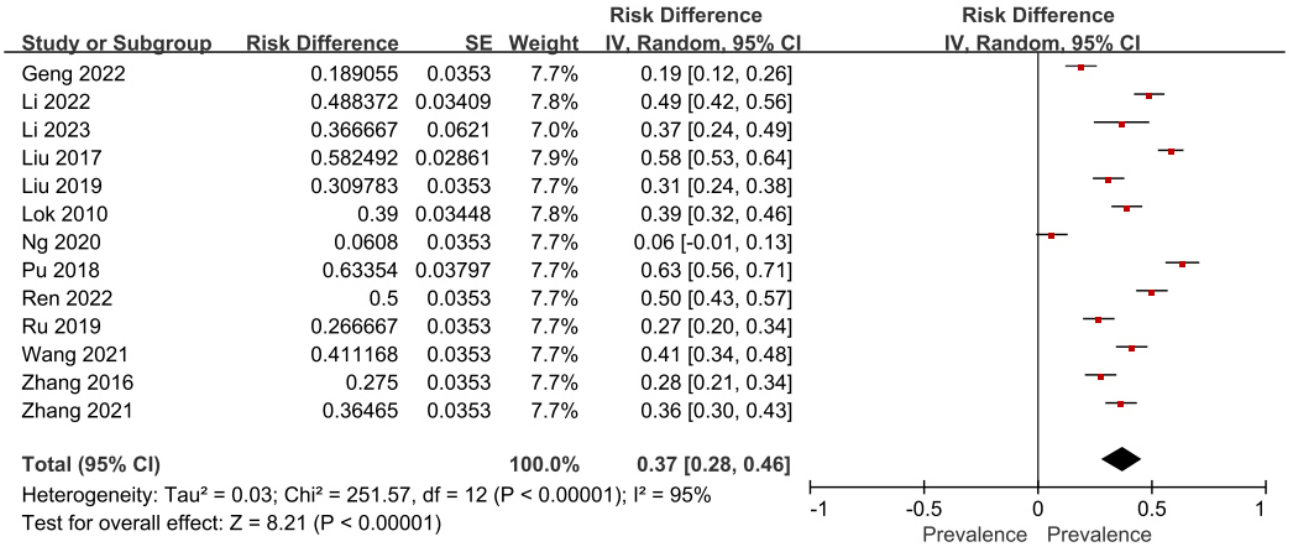

Fig. 2. The pooled depression prevalence in patients with rheumatoid arthritis. SE, Standard Error; CI, Confidence Interval; df, degree of freedom; IV, Inverse Variance.

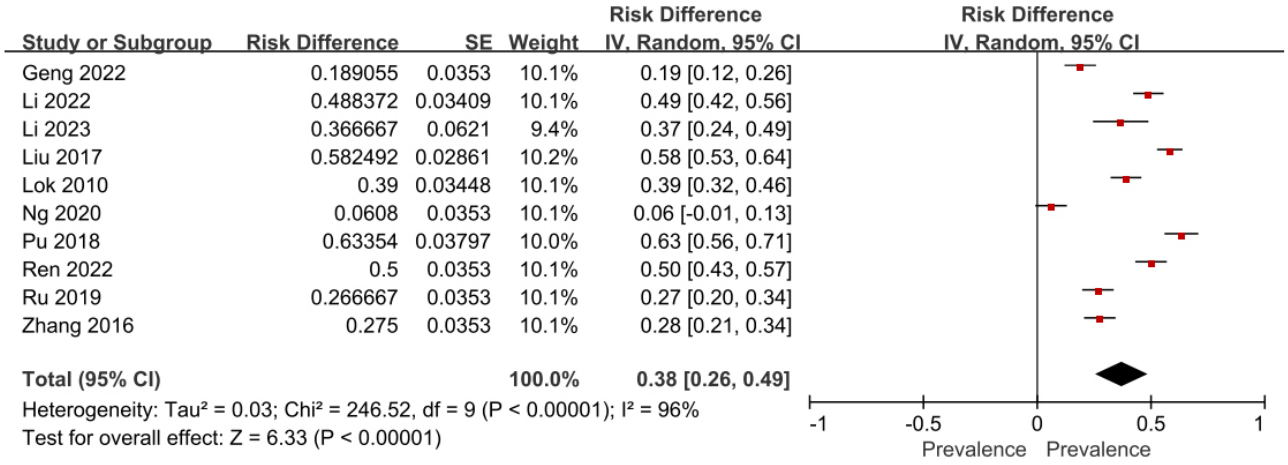

Fig. 3. The pooled depression prevalence in patients with rheumatoid arthritis (published in English). SE, Standard Error; CI, Confidence Interval; df, degree of freedom; IV, Inverse Variance.

Table 2. Results of subgroup analysis based on scale type and age.

	Number of studies	Sample size	Prevalence, % (95% CI)	Pooled OR	*p*-value	Heterogeneity	
						I^2, %	*p*-value
Scale type							
HAMD	3	436	50% (37–64)	4.93 [1.79–10.2]	<0.0001	87	0.018
HADS	3	27,983	35% (29–46)	1.62 [0.76–3.24]	0.0600	65	0.021
CES-D	1	297	58% (53–64)	2.83 [1.71–4.65]	<0.0001	-	-
DSM criteria	1	200	39% (32–46)	0.75 [0.38–1.51]	<0.0001	-	-
SDS	1	197	41% (34–48)	0.95 [0.32–2.16]	<0.0001	-	-
Mean age, years							
≥50	8	1879	41% (32–51)	1.25 [0.59–2.70]	<0.0001	94	0.007
<50	5	26,609	48% (32–65)	1.99 [0.93–3.81]	<0.0001	92	0.026

CI, Confidence Interval; OR, Odds Ratio; HAMD, Hospital Anxiety and Depression; HADS, Hamilton Depression Scale; CES-D, Center for Epidemiologic Studies Depression; DSM, Diagnostic and Statistical Manual of Mental Disorder; SDS, Self-Rating Depression Scale.

The study categorized participants into two age groups: ≥50 and <50 years old. Eight studies established an average age of ≥50 years old, with a total sample size of 1879 and a depression incidence of 41% (95% CI: 32–51%). Five studies established an average age of <50 years old, totaling a sample size of 26,609 and a depression incidence of 48% (95% CI: 32–65%).

The depression prevalence showed significant associations with the HAMD scale (OR 4.93, 95% CI: 1.79–10.2), CES-D scale (OR 2.83, 95% CI: 1.71–4.65), DSM.IV (OR 0.75, 95% CI: 0.38–1.51), SDS (OR 0.95, 95% CI: 0.32–2.16), age ≥50 (OR 1.25, 95% CI: 0.59–2.70), and age <50 (OR 1.99, 95% CI: 0.93–3.81).

The Subgroup Analysis Based on Gender

Table 3 presents the incidence of depression by gender. For the 24,408 female individuals with RA, the comprehensive depression incidence was 45% (95% CI: 37–55%). In contrast, the overall incidence of depression for the 4705 male individuals with RA was 39% (95% CI: 29–48%). Compared to males with RA, females exhibited a significantly higher overall incidence of depression. The depression prevalence was significantly associated with females (OR 1.63, 95% CI: 0.64–4.57) and males (OR 1.07, 95% CI: 0.38–3.03).

Discussion

Rheumatoid arthritis (RA) is a chronic progressive autoimmune disease that can lead to limb pain and movement disorders, impacting individuals' emotions and quality of

Table 3. Results of subgroup analysis based on gender.

Gender	Number of studies	Sample size	Prevalence, % (95% CI)	Pooled OR	*p*-value	Heterogeneity	
						I^2, %	*p*-value
Female	13	24,408	45% (37–55)	1.63 [0.64–4.57]	<0.0001	92	0.022
Male	13	4705	39% (29–48)	1.07 [0.38–3.03]	<0.0001	71	0.015

CI, Confidence Interval; OR, Odds Ratio.

life. The recurrent acute episodes of RA may exacerbate individuals' psychological and mental health issues [32]. Notably, individuals with RA may experience symptoms associated with depression, such as fatigue, loss of appetite, and poor sleep, potentially contributing to a higher depression prevalence [33]. This study aims to examine the prevalence of depression among Chinese individuals diagnosed with RA. The results indicated an overall depression incidence of 37% (95% CI: 28–46%; $I^2 = 95\%$; $p < 0.0001$), based on a comprehensive analysis of 13 studies involving 29113 Chinese individuals with RA. This significant prevalence disparity suggests a higher risk of depression in RA patients compared to the general population [34]. Another study indicated that RA patients have a 47% higher risk of depression than those without RA, emphasizing the potential contribution of RA to an increased risk of depression [35].

Interestingly, this study found varying prevalence rates of depression based on the type of questionnaire used, with the HAMD scale, HADS, CES-D scale, DSM.IV diagnostic criteria, and SDS scale resulting in rates of 50%, 35%, 58%, 39%, and 41%, respectively. These findings highlight the importance of considering different assessment tools when examining depression rates in individuals with RA. Moreover, the study revealed gender-based differences in depression prevalence among those with RA, reporting rates of 45% (95% CI: 37–55%) in females and 39% (95% CI: 29–48%) in males. Comparatively, the general population in China reported a lower depression prevalence of 3.4%, with higher rates observed among adult females (4.2%) compared to males (3.0%) [36]. The higher prevalence of depression among female Chinese individuals with RA further emphasizes the need for targeted mental health interventions within this population. Future research should focus on identifying potential factors contributing to this association and developing effective strategies to address the mental health needs of RA patients. Discrepancies in reported depression rates among various RA populations, spanning from 9.5% to 41.5%, may be attributed to variations in study populations and depression definition criteria [37]. Moreover, studies with larger sample sizes and longer durations are more likely to provide accurate estimates of depression prevalence compared to smaller, shorter-term studies. Population characteristics such as age, gender, ethnicity, socioeconomic status, and disease severity can significantly influence the reported rates of depression in individuals with RA. Additionally, variations in diagnostic criteria employed by researchers, differences in assessment tools and measures used to evaluate depression can also contribute to inconsistencies in the reported rates. For instance, a previous study included the research data of 13188 individuals with RA in 72 studies, establishing a depression prevalence of 38.8% (95% CI: 34–43%) and a 16.8% prevalence of severe depressive disorder [11]. Comparatively, a Chinese study suggested that the depression prevalence among individuals with RA was 48% (95% CI: 41–56%), with an 18% prevalence of moderate and severe depression [38]. Notably, the latter study [37] included more English publications.

In the subgroup analysis, we observed significant associations between depression prevalence and the HAMD scale (OR 4.93, 95% CI: 1.79–10.2), CES-D scale (OR 2.83, 95% CI: 1.71–4.65), DSM.IV scale (OR 0.75, 95% CI: 0.38–1.51), SDS (OR 0.95, 95% CI: 0.32–2.16), age ≥50 (OR 1.25, 95% CI: 0.59–2.70), age <50 (OR 1.99, 95% CI: 0.93–3.81), female gender (OR 1.63, 95% CI: 0.64–4.57) and male gender (OR 1.07, 95% CI: 0.38–3.03). Gender-specific variations in depression rates have been noted, with a study targeting community residents in multiple countries suggesting a significantly higher lifetime severe depression prevalence in females compared to males (1.9 times), potentially arising from different causes of depression [39]. Gender-specific differences in depression are linked to differences in estrogen and androgen levels [40]. Additionally, age appears to be a factor influencing the depression incidence among Chinese individuals diagnosed with RA, with higher rates observed in those below 50 years old compared to those aged 50 years or above. Considering the average age of the participants, the present study found that the incidence of depression among Chinese individuals with RA aged ≥50 years and <50 years was 41% (95% CI: 32–51%) and 48% (95% CI: 32–65%), respectively. These results suggest that, compared to Chinese RA individuals ≥50 years, individuals with an average age of <50 years have a higher incidence of depression. Similar patterns have been observed in the general population,

where severe depression prevalence in younger individuals is significantly higher (11–13% vs 5%) compared to those aged 65 and older [41].

Furthermore, variations in depression prevalence may be influenced by the use of different scales and diagnostic criteria [42]. In our investigation, we analyzed several studies that employed different scales to measure various variables related to our research question. The use of diverse scales across different studies is not uncommon in academic research, as researchers often select scales based on their specific research objectives and the study context. Upon careful examination, we identified variations and notable similarities in the scales used across the studies. Despite slight variations in wording and response options, the underlying concepts being measured were consistent across the studies. This indicates a certain level of convergent validity, suggesting that the different scales were assessing similar aspects of the phenomenon under investigation. Moreover, there is a possibility of file drawer effects, as researchers and publishers tend to favor studies with significant findings, potentially creating a publication bias toward positive results. Consequently, studies with null or inconclusive results might not be published or made publicly available, resulting in an incomplete representation of the research landscape. To address this possibility, it is crucial for researchers to conduct comprehensive literature searches, including unpublished studies and gray literature, such as conference proceedings and dissertations. The study highlighted the anxiety and depression burden of patients with rheumatoid arthritis. Beyond medication and biological state, attention to the patient's mental state is essential and may influence treatment efficacy. Improving patients' anxiety and depression status in the future could contribute to the management of rheumatoid arthritis patients and enhance their prognosis. This study had the following limitations. Firstly, despite efforts to minimize bias in the selection of the study population, most included studies are single-center studies focused on the hospital population. Therefore, caution should be exercised when extrapolating the results. Secondly, compared to other large-scale surveys, the sample size of this study is considerably smaller. Thirdly, different scales were applied among the included studies, leading to variations in diagnostic performance, sensitivity, and specificity, which could consequently cause inconsistencies in depression prevalence. Lastly, this study only counted the overall incidence of depression and did not differentiate the severity of depression.

Conclusion

In conclusion, the depression prevalence was high in Chinese individuals with RA, especially in females and those <50 years old. This indicates that the detection and management of depression in individuals with RA require attention. Healthcare practitioners and researchers should conduct comprehensive assessment, treatment, and long-term management of depression in individuals with RA through interdisciplinary collaboration, aiming to improve the overall well-being and quality of life of this population.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

JH contributed to the concept and designed the research study. WC performed the research. PZ contributed to the analysis and interpretation of the data. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

Not applicable.

Acknowledgment

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://actaspsiquiatria.es/index.php/actas/article/view/1536.

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