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Bidirectional Association between Arthritis and Mental Health- A Review

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ABSTRACT
Arthritis and mental health, particularly depression, share a complex and bidirectional relationship that significantly impacts patient well-being and healthcare outcomes. This comprehensive review examines the multifaceted interplay between arthritis and mental health, highlighting the mechanisms, impacts, interventions, controversies, and gaps in current research. Arthritis, encompassing various types such as osteoarthritis, rheumatoid arthritis, and psoriatic arthritis, contributes to depression, anxiety, and distress, while mental health issues can exacerbate arthritis symptoms. Mechanisms underlying this association involve inflammatory pathways, neuroendocrine dysregulation, and psychosocial factors. Mindfulness-based interventions, cognitive-behavioural therapy, and tailored psychological support show promise in alleviating symptoms and enhancing coping strategies. However, controversies exist regarding causality and treatment outcomes, necessitating further research to elucidate underlying mechanisms, assess treatment impacts, and develop more effective interventions. By addressing this bidirectional relationship comprehensively, healthcare providers can enhance patient well-being, optimize treatment adherence, and improve overall health outcomes.
KEYWOORDS: - Arthritis, Mental health, Depression, Rheumatoid arthritis, Anxiety, Bidirectional relationship

I. INTRODUCTION

Arthritis, a condition marked by inflamed joints, significantly restricts mobility and daily activities, leading to chronic pain and a decline in well-being. The presence of arthritis can restrict participation in work and daily activities, leading to a loss of independence and a diminished quality of life [1].Arthritis presents a broad array of symptoms, such as pain, stiffness, restricted movement, and changes in joint morphology. The realm of arthritis encompasses over a hundred distinct variations, among which are osteoarthritis, rheumatoid arthritis, and psoriatic arthritis [2]. Numerous studies have suggested that rheumatoid arthritis (RA), psoriatic arthritis (PA), and osteoarthritis (OA), are correlated with diminished quality of life and heightened disability [3].

The negative impact of arthritis on mental health is a growing concern [4]. Depression emerges as a prevalent mental health condition among the elderly population, exerting a noteworthy adverse effect on their overall quality of life [5]. The frequent co-occurrence of RA and depression suggests a potential causal association, which could be mediated by a malfunctioning neuroendocrine system [6, 8].In 2017, depression contributed to 43 million years lived with disability (YLD) based on global data analysis [5].Recent research has prioritized understanding how arthritis shapes individuals' perceived necessity for and utilization of mental healthcare, revealing an augmented perceived need for mental healthcare within the arthritis demographic, notably among males [9].

A study exploring the interplay between depression and arthritis unveiled that individual living with depression had a 1.56 times higher likelihood of developing arthritis in comparison to individuals without depression [10].A substantial-scale research endeavour involving over 7,300 participants monitored over an extended period (prospective study) established a significant association between arthritis and a heightened propensity for developing depression. Specifically, they exhibited a 35% heightened risk of experiencing depression for the first time (incident depression) and a 50% increased risk ofdeveloping long-term depression (persistent depression) compared to the group without arthritis [1].

Through a cohort study, researchers observed an elevated susceptibility to depressive disorders among patients diagnosed with gout. The study findings demonstrated a significant disparity in the frequency of depression, with a higher prevalence observed in the gout cohort in contrast to the non-gout cohort [11].Arthritis can directly

International Journal of Pharmaceutical Research and Applications
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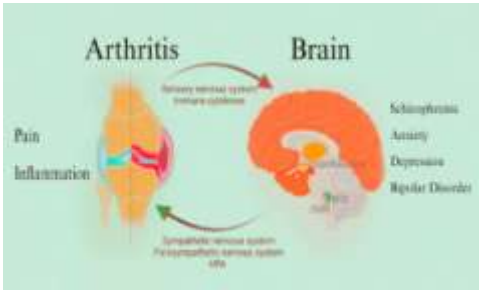
trigger or worsen anxiety and distress, highlighting the importance of holistic care for this condition. Despite the predominant focus on depression in the clinical discourse surrounding arthritis, it's important to recognize that anxiety is nearly twice as prevalent among affected individuals. This finding suggests that anxiety may be a more prominent concern than depression among people with arthritis.

In a study of 1,793 individuals, 31% reported anxiety compared to 18% with depression. Additionally, 33% indicated experiencing at least one of these conditions. The majority of individuals, comprising 84%, who experienced depression also concurrently presented with comorbid anxiety. Even though a high percentage (84%) of people with depression also had anxiety. Furthermore, only half of the respondents with anxiety or depression sought mental healthcare in the past year [12].

Based on data from the National Survey on Drug Use and Health (NSDUH), there was a documented uptick in the occurrence of depression among adolescents, escalating from 8.3% to 12.9% between 2011 and 2016 [13].Chronic illnesses in children are linked to an elevated risk of experiencing anxiety and depression compared to healthy children [14-16].Furthermore, longitudinal studies indicate that children with chronic diseases experience less favourable trajectories concerning their mental health symptoms over time [17].

According to a systematic review, children suffering from juvenile idiopathic arthritis (JIA) commonly manifest symptoms indicative of depression and anxiety, mirroring the patterns seen in other chronic paediatric conditions, and surpassing prevalence rates observed in healthy children. Highlighting the study's findings, it was revealed that depression and anxiety symptoms significantly compromise the quality of life within individuals in the context of juvenile idiopathic arthritis (JIA), suggesting that these psychological factors might wield a greater influence compared to specific disease markers like active joint count [18].Distress, manifested in conditions like depression and anxiety, is a major concern for people living with rheumatoid arthritis. Studies highlight the critical need to understand and address DSD, a unique form of psychological distress experienced by RA patients. In response to the growing recognition of disease-specific distress (DSD) in RA, tools like the Rheumatoid Arthritis Distress Scale (RADS) have been developed to recognize and quantify this unique form of emotional burden [19,20].

Through a comprehensive review, we delve into the bidirectional association between mental health and arthritis, revealing how each significantly affects the other. This insight underscores the necessity for integrated healthcare approaches, acknowledging the reciprocal impact on mental well-being and arthritis outcomes, thereby informing the development of more holistic interventions.



I.1 Bidirectional relationship between Arthritis and Mental Health

II. IMPACT OF MENTAL HEALTH ON ARTHRITIS

The pathogenesis of rheumatoid arthritis (RA) involves an immune system malfunction characterized by the over expression of critical inflammatory mediators such as tumour necrosis factor-α (TNFα), interleukin-6 (IL6), and interleukin-1β (IL-1β). These abnormalities signify Dysfunctional inborn and adaptive immune processes, contributing to the disease's inflammatory nature [21, 22].Levels of interleukin-1 receptor antagonist (IL-1ra), a molecule that can indicate the activity of interleukin-1β (IL-1β), have been consistently linked to depression [23].Poor mental health can significantly worsen various aspects of arthritis for patients. Conditions like depression and anxiety can hinder treatment effectiveness and worsen disease activity in arthritis patients, especially those with rheumatoid arthritis (RA) [24].

Studies strongly suggest that depression can worsen the trajectory of rheumatoid arthritis (RA) [25].In addition to its impact on disease activity, depression amplifies complications associated with arthritis, amplifies pain perception, and is associated with diminished odds of attaining remission, resulting in a decrease in overall health-associated quality of life [26,27]. Furthermore, there exists a correlation between depression and heightened mortality rates in individuals with

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rheumatoid arthritis (RA), with studies estimating that approximately 6.9% of mortality in RA patients can be attributed to depression [28].The presence of depression might intensify the inflammatory aspects inherent in rheumatoid arthritis (RA), thereby playing a role in amplifying disease activity [29].Prolonged exposure to ongoing psychosocial stressors has been linked to heightened inflammation via the activation of inflammasomes, which in turn may precipitate adverse psychological and physiological consequences in individuals grappling with mental health conditions [30, 31].

Researchers conducted a long-term observational study (prospective longitudinal study) to evaluate whether increased psychological support improves pain management, reduces disability, and enhances mental well-being in adolescents recently diagnosed with juvenile idiopathic arthritis (JIA).The results of the study highlight the need for further exploration in this area [32].Abdul-Sattar and colleagues discovered that more than 75% of patients exhibiting notable symptoms of depression encountered a diminished quality of life [33].According to recent studies, young people diagnosed with Juvenile Idiopathic Arthritis (JIA) often show clinically relevant symptoms of anxiety and depression. This prevalence is similar to what's observed in other chronic childhood illnesses, and potentially even higher compared to healthy children [34]. The presence of depression and anxiety has been linked to the modulation of specific disease factors in juvenile idiopathic arthritis (JIA [34].The emergence and persistence of pain in individuals previously considered healthy have been identified as contributors to adverse changes in both their physical and mental well-being [35, 36].Santos and colleagues validated an indirect association between disease activity and the manifestation of symptoms of depression, which was mediated through various impact of the disease factors including pain, functional disability, physical well-being, and coping mechanisms [37].

Anxiety and depression significantly diminish the quality of life (QoL) for patients, with findings suggesting that individuals with psoriatic arthritis experience notably poorer QoL compared to counterparts with conditions like rheumatoid arthritis. This underscores the possibility that the presence of skin manifestations, in addition to joint involvement, could heighten psychological distress [38].Depression is a prevalent mental health concern among older adults, significantly diminishing their overall well-being [39].A review of available long-term studies (longitudinal studies) on depression and RA suggests a potential link between depression and both worsened disease activity and increased pain.

However, the exact reasons for these connections remain unclear [40].A study conducted by Peterson et al. showed that patients with RA who also had anxiety or depression experienced a more substantial decrease in their health-related quality of life and faced greater economic burdens compared to those without these mental health conditions [41].Mental health issues can influence the assessment of disease activity, with individuals suffering from rheumatoid arthritis (RA) and concurrent depression or anxiety potentially reporting higher disease action levels than their physicians [42].The majority of research investigating the mental health aspects of rheumatoid arthritis (RA) has primarily concentrated on depression.

A systematic literature review analysing seven research articles, albeit of low to moderate quality, suggests a possible link between depression and heightened disease activity in RA patients [43].Research on anxiety in RA has often focused on its co-occurrence with depression. One example is an examination of data from a randomized controlled trial (RCT) through a secondary analysis. This analysis investigated whether symptoms of depression and anxiety, measured using EQ-5D tool, could predict a patient's response to treatment [44].The research revealed a notable correlation between both initial and ongoing (persistent) mood problems with higher DAS28 scores. Understanding the percussion of anxiety on quality of life (QoL) and activity of disease in rheumatoid arthritis (RA) is essential for providing empirical support for the acknowledgement and appropriate anxiety management in RA patients [45].Major psychiatric disorders like depression and anxiety are frequently linked to rheumatoid arthritis (RA), with their origins attributed to either biological pathways involving cytokines or the psychological strain caused by the ongoing medical hardships experienced by patients [46].

III. IMPACT OF ARTHRITIS ON MENTALHEALTH

Numerous research investigations have underscored the detrimental influence of arthritis on mental health, encompassing both broad mental health indices and specific dimensions. Findings

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consistently highlight the role of pain, fatigue, and inflammation in exacerbating mental health challenges among individuals with arthritis. Notably, affected individuals commonly report symptoms such as social dysfunction, anhedonia, depression, anxiety, and a decline in self-assurance, which significantly compromises their overall mental well-being [4]. Rheumatoid arthritis (RA) significantly, reduces individual's overall well-being due to pain, fatigue, and limitations in everyday tasks (disability). This can lead to negative emotional consequences, such as anxiety and depression. Compared to the general population, individuals with rheumatoid arthritis (RA) are at a higher risk of developing these conditions, along with cognitive decline. To develop the most effective treatment plans, healthcare providers need to consider the influence of mental health on RA disease activity [24].People having inflammatory arthritis experience a higher risk of developing mental health problems and a decrease in their overall quality of life.

Conversely, the interplay between arthritis and mental health has become a central focus of research, as evidenced by numerous academic works exploring this complex relationship. Findings from a study revealed that person living with arthritis perceive a higher necessity for mental health interventions, while demonstrating similar probabilities of accessing mental healthcare services in comparison to those not affected by arthritis. The study revealed a noteworthy gender disparity, indicating that men afflicted with arthritis exhibited considerably elevated odds of recognizing a need for care when compared to their female counterparts. The study underscores the critical role of routinely assessing mental health needs in people with arthritis [9].In a community-based research endeavour, it became evident that arthritis is closely affiliated with heightened levels of various mental health maladies, spanning depression, anxiety, and disturbances in sleep, elevated stress levels, and manifestations of psychosis. The study underscores the importance of routinely assessment for mental health conditions in people having arthritis to ensure they receive appropriate interventions [47].The disruption of clinical care services during the COVID-19 pandemic has been associated with adverse short-term mental health outcomes, according to various studies. For optimal care in inflammatory arthritis, regular monitoring of both mental health and quality of life is crucial [48].

IV. MECHANISM

4.1 MECHANISM OF ARTHRITIS IN MENTAL HEALTH

Co-occurring depression is a prevalent occurrence among patients diagnosed with rheumatoid arthritis (RA), often resulting in detrimental health consequences. Socioeconomic disadvantage has been notably recognized as a significant contributing factor to this phenomenon [49].RA patients with depression often exhibit weaker coping skills, particularly during disease flares. This can negatively impact their health-seeking behaviours and overall healthcare utilization [50].Furthermore, depression in RA patients can distort their perception of illness severity. This can manifest as a heightened experience of pain, fatigue, and physical limitations, potentially hindering medication adherence and compromising overall health outcomes [50].Engaging in proactive self-management practices within rheumatoid arthritis (RA) has been correlated with elevated levels of treatment adherence. Despite the potential for treatment goals not being fully attained, this adherence often translates to improved patients' outcomes [48].

RA patients with increased levels of acute-phase reactants and proinflammatory cytokines, markers of systemic inflammation, demonstrate a higher risk of developing depression [49, 51].Elevated levels of acute-phase reactants and inflammatory cytokines are commonly observed in individuals experiencing symptoms of depression. Moreover, depressed patients often exhibit heightened concentrations of various cytokines, adhesion molecules, and chemokines [49, 51].High levels of certain cytokines, including tumour necrosis factor-alpha (TNF-α), and interleukin-6 (IL-6) might be indicative of a poor response to treatment for depressive symptoms. This finding suggests a potential connection between inflammation and treatment outcomes in depression [49, 51].This suggests a reciprocal relationship between depression andrheumatoid arthritis (RA), fostering a detrimental cycle of RA exacerbating depressive symptoms, and vice versa, ultimately leading to compromised health outcomes [46,51].

4.2 MECHANISM OF MENTAL HEALTH IN ARTHRITIS

Rheumatoid arthritis (RA) is marked by an increase in key proinflammatory cytokines, includinginterleukin-6 (IL-6), interleukin-1β (IL-1β),and tumour necrosis factor-alpha (TNFα). This

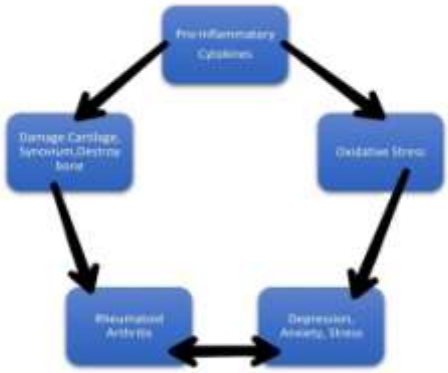
International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 2 Mar-Apr 2024, pp: 1192-1202 www.ijprajournal.com ISSN: 2249-7781

suggests a dysregulation within the innate and adaptive immune system component [19].

Systemic inflammation has been linked with the onset of depressive symptoms in a range of severe inflammatory illnesses, containing chronic obstructive pulmonary disease (COPD) and diabetes mellitus suggesting a common mechanism underlying the development of depression in these conditions [14].

Inflammatory cytokines possess the ability to cross the central nervous system (CNS) via two routes: the humoral pathway and the neural pathway. Through the route of humoral, cytokines breach the blood-brain barrier (BBB), which undergoes permeabilization because of the presence of circulating mediators. Transport molecules, such as TNFα, are instrumental in facilitating the transportation of cytokines through the blood-brain barrier and into the CNS [23].

This process suggests a potential mechanism by which systemic inflammation associated with RA may impact mental health, including the development of depression's symptoms.



4.2.1 Mechanism of Arthritis & Mental illness and association between Arthritis and Mental Health

V. QUALITY OF LIFE

Rheumatoid arthritis (RA) is a persistent autoimmune condition marked by widespread inflammation within the body. This persistent inflammation led to progressive damage in joint and a substantial decline in a patient's quality of life [4].Rheumatoid arthritis (RA) can significantly diminish life quality due to fatigue, pain, and limitations in daily activities (disability). This can lead to negative emotional consequences, such as anxiety and depression [11, 12].

Depression plays a major role in the increased occurrence of suicidal ideation within the rheumatoid arthritis (RA) patient population. The presence of this mood disorder amplifies the likelihood of experiencing thoughts of self-harm or suicide among individuals living with RA [17].The presence of depression in Rheumatoid Arthritis patients appears to be associated with several negative outcomes. The findings suggest a link between depression and: Lower rates of achieving clinically significant remission of Rheumatoid Arthritis symptoms, Heightened pain levels, Greater functional limitations, A decline in overall quality of life, Increased mortality risk [29,39].Depression has been proven to have a substantial negative impact on the well-being of individuals diagnosed with rheumatoid arthritis (RA) [5, 9].Prolonged or persistent depression is linked to considerable declines in the quality of life and an elevated risk of experiencing suicidal thoughts or ideation [55].The combined presence of rheumatoid arthritis (RA) and anxiety or depression can create a compounding effect, leading to a more significant decrease in quality of life for RA patients [20].

Concurrent anxiety and depression in RA patients are significant risk factors for poorer quality of life, increased suicidality, and a worse prognosis for the disease itself [2].It was a prevalent discovery among patients and exerted a notable effect on their overall quality of life [19].In their review, Fair et al. (2019) analysed 28 articles published between 2009 and 2019. The majority (75%) concentrated on the frequency of depression in JIA patients, while half examined anxiety prevalence. Notably, less than a third of the studies investigated the link between mental health and either JIA disease characteristics or the impact on patients' quality of life [10].

VI. INTERVENTION

According to Irwin et al. (2008), mindfulness-based interventions (MBIs) may be a promising approach for managing pain and improving well-being in RA patients with recurrent depression. This research suggests that MBIs could be even more effective than standard treatments like cognitive-behavioural therapy (CBT) for this specific patient population [6].For RA patients with a history of depression, incorporating interventions that focus on emotional regulation and self-management skills could be particularly beneficial. This emphasizes the crucial role of addressing

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mental health alongside physical symptoms in comprehensive RA management [6].

Effective intervention strategies for the interrelated aspects of arthritis and mental health require acknowledging this two-way street and implementing targeted approaches for each condition.RA and depression appear to be linked in a two-way cycle, increasing each other's risk. This emphasizes the need for early detection of both conditions [56, 57].In addressing the reciprocal link between rheumatoid arthritis (RA) and depression, healthcare providers must implement diverse intervention approaches aimed at enhancing overall well-being, encouraging adaptive coping mechanisms, and delivering timely therapeutic interventions for both conditions. This emphasizes the necessity of a comprehensive care plan tailored to tackle the multifaceted challenges posed by RA and depression [57].A multi-pronged approach to mental health in rheumatology care can significantly improve outcomes. This includes: Early detection through routine screening, Prevention for high-risk patients, combined treatment plans for RA and depression [58].Research suggests that psychological interventions can be a valuable alternative, or complement, to medication-based pain relief in managing the complicated relationship between mental health issues and chronic pain [59].

Understanding the complex relationship between arthritis and mental health enables tailored interventions for improved well-being. Moving forward, interventions for mental health in arthritic patients must go beyond the clinical realm [60]. A comprehensive approach should acknowledge the challenges of controlling arthritis and integrate strategies to consider the social aspects of treatment [61, 62].

VII. CONTROVERSIES AND GAP

Despite growing evidence for a two-way relationship between arthritis, particularly rheumatoid arthritis (RA), and depression, research in this area continues to evolve. Some controversies remain, and there are gaps in knowledge that need to be addressed. A key area of debate surrounds the precise nature of the linkage between depressive symptoms (DS) and knee osteoarthritis (KOA).Although research suggests a two-way connection between depressive symptoms (DS) and knee osteoarthritis (KOA), the exact mechanisms and causal direction of this relationship remain a topic of debate [58, 64].While some scholars contend that the chronic inflammatory processes linked with arthritis may contribute to the development of depression, others argue that depression might exacerbate arthritis symptoms due to compromised stress-coping behaviours [64].

A separate area of debate centres on the extent to which mental health conditions, like depression, influence the activity of disease itself in RA.Research suggests a link among depression in RA patients and a more severe disease course, potentially leading to poorer health outcomes. Despite evidence suggesting a reciprocal relationship, the precise biological pathways through which mental health conditions like depression impact RA progression, and vice versa, remain unclear [64, 49].

Furthermore, there remains an evident dearth of research centered on how the severity of arthritis and various treatment approaches impact mental health outcomes, indicating a significant gap in the existing literature that requires attention and investigation. A notable limitation in existing research lies in the insufficient documentation of arthritis severity levels and treatment particulars, complicating efforts to discern the influence of these factors on the likelihood of experiencing depressive symptoms or other mental health challenges [58].

The research papers offered shed light on the mutually influential connection between arthritis and mental health, notably depression, highlighting the complex and bidirectional nature of their association. A key finding from one study was the independent association between depression and arthritis. This suggests that the two conditions can influence each other even when considering factors like socioeconomic status, age, health behaviours, and overall health status [10].Another research investigation concentrated on rheumatoid arthritis (RA) and depression, accentuating a mutual relationship between these ailments, particularly prevalent among the elderly demographic, with implications for elevated mortality risks [3].

Additionally, advancements in research have contributed to a better understanding of how mental health influences rheumatoid arthritis (RA) disease activity, signifying notable progress in this area of study. Studies have highlighted that individuals diagnosed with both rheumatoid arthritis (RA) and depression encounter greater difficulties in maintaining biological function, emphasizing the imperative of addressing mental health considerations within arthritis patient care [49].Additionally, researchers utilized a two-sample

International Journal of Pharmaceutical Research and Applications
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Mendelian randomization design to explore the bidirectional links between mental illness and rheumatoid arthritis, employing genetic variants as instrumental variables to uncover insights into their mutually influential dynamics. This Mendelian randomization (MR) study specifically investigated the potential causal influences of bipolar disorder, anxiety, and depression on the development of RA. The findings aimed to shed light on the complex link between these mental health conditions and the risk of developing RA [65].

VIII. CONCLUSION

In conclusion, the bidirectional relationship between arthritis and mental health, particularly depression, underscores the intricate interplay between these conditions and highlights the importance of integrated healthcare approaches. Arthritis significantly impacts mental well-being, contributing to depression, anxiety, and distress, while mental health issues can exacerbate arthritis symptoms, leading to increased pain, disability, and decreased life quality. The mechanisms at play in this association involve complex interactions between inflammatory pathways, neuroendocrine dysregulation, and psychosocial factors. Interventions targeting both arthritis and mental health are essential for improving patient outcomes, with mindfulness-based interventions, cognitive-behavioral therapy, and tailored psychological support showing promise in alleviating pain, enhancing well-being, and promoting adaptive coping strategies. However, further research is warranted to elucidate the underlying pathways, explore the impact of arthritis severity and treatment modalities on mental health outcomes, and develop more effective interventions. By addressing the bidirectional relationship betweenmental health and arthritis, healthcare providers can enhance patient well-being, improve treatment adherence, and optimize overall health outcomes.

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