e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2024; 16(4): 10-14

Original Research Article

Psychiatric Symptoms in Primary Fibromyalgia and Fibromyalgia Secondary to Rheumatoid Arthritis: A Comparative Study

Rahul Mishra[1], Jeetandra Kumar Sharma[2], Vinay Kumar Oddam[3], Pradeep Kumar Pathak[4], Bhavna Chopra[5], Rupesh Kumar Gupta[6]

[1]Associate Professor, Department of Psychiatry, Birsa Munda Government Medical College, Shahdol, Madhya Pradesh, India

[2]Assistant Professor, Department of Medicine, Birsa Munda Government Medical College, Shahdol, Madhya Pradesh, India

[3]Assistant Professor, Department of Orthopaedics, Birsa Munda Government Medical College, Shahdol, Madhya Pradesh, India

[4]Assistant Professor, Department of Orthopaedics, Birsa Munda Government Medical College, Shahdol, Madhya Pradesh, India

[5]PGMO SNCU/PICU, KushaBhau Thakrey District Hospital, Shahdol, Madhya Pradesh, India

[6]Associate Professor, Department of Medicine, Birsa Munda Medical College, Shahdol, Madhya Pradesh, India

Received: 03-02-2024 Revised: 11-03-2024 / Accepted: 05-04-2024

Corresponding author: Dr. Pradeep Kumar Pathak

Conflict of interest: Nil

Abstract

Introduction: Fibromyalgia (FM) is a common occurrence among patients diagnosed with rheumatoid arthritis (RA). Our study aimed to assess the variations in psychiatric comorbidities and life challenges between individuals with Rheumatoid arthritis plus FM (secondary fibromyalgia [SFM]) and those with primary FM (PFM).

Materials and Methods: We recruited 45 patients with PFM and 53 with SFM for the study. This cross-sectional, observational study involved structured interviews with patients diagnosed with PFM and SFM to determine lifetime occurrences of major depression (MDD), panic disorder (PD), and post-traumatic stress disorder (PTSD). Additionally, participants were evaluated for childhood/adulthood adversities and the severity of FM-related symptoms.

Results: Univariate analysis revealed significantly higher lifetime rates of MDD in PFM compared to SFM, as well as higher rates of PD, with no notable difference in PTSD rates. Furthermore, rates of sexual abuse and physical neglect were notably higher in PFM patients than in SFM patients. Life events occurring before the onset of FM differed between the PFM and SFM groups. In the logistic regression model, lifetime PD and physical neglect emerged as independent risk factors for PFM.

Conclusion: These findings indicate that PFM and SFM exhibit differences in psychiatric comorbidities and environmental adversities, suggesting that a common pathogenesis may manifest through distinct pathways.

Keywords: Fibromyalgia, Psychiatric disorders, Rheumatoid arthritis, Stress.

Introduction

Rheumatoid arthritis (RA) is a persistent inflammatory condition characterized by pain, stiffness, and swelling in peripheral joints. Joint pain typically manifests in areas like the hands, wrists, and feet, occasionally extending to other joints such as elbows, shoulders, neck, knees, ankles, or hips. Traditionally, this pain has been attributed to peripheral inflammation. However, with the advent of biological and non-biological disease-modifying anti-rheumatic drugs (DMARDs) that effectively manage peripheral inflammation, many patients have experienced improved functionality and reduced pain as they age. Nonetheless, up to 50% of individuals continue to report clinically significant levels of pain despite effective inflammation control [1].

The persistence of pain despite indicators of good control over inflammatory processes, as evidenced by clinical, radiological, and laboratory assessments [2, 3], has led to the hypothesis that factors beyond peripheral inflammation contribute to patients' pain experiences. Central sensitization, characterized by heightened responsiveness of neurons in the central nervous system (CNS) to normal or sub-threshold stimuli, is considered a fundamental mechanism in chronic musculoskeletal

pain, such as that seen in fibromyalgia (FM). FM presents not only with pain but also with fatigue, sleep disturbances, cognitive impairment, and psychiatric symptoms like depression and anxiety disorders.

FM and RA share common clinical features such as pain and tenderness at multiple musculoskeletal sites. Epidemiological studies suggest that FM occurs in about 20% of RA patients, a much higher rate compared to the general population's 1%-4% prevalence of FM [4, 5]. Moreover, FM is frequently associated with various chronic conditions with structural pathology, including systemic lupus, ankylosing spondylitis, osteoarthritis, and psoriatic arthritis, as well as endocrine disorders like autoimmune thyroid disease and diabetes mellitus [6]. Additionally, individuals may exhibit FM-related symptoms in response to illness or psychosocial stressors, known as 'fibromyalgianess' (FMness). While FMness can coexist with many chronic diseases, FM itself is recognized as a distinct diagnostic entity with autonomous clinical significance since the American College of Rheumatology (ACR) classification criteria were established in 1990 [7]. Subsequent criteria in 2016 further delineate FM as a multi-symptomatic disorder with high rates of comorbidity, particularly with psychiatric conditions like major depressive disorder (MDD) and panic disorder (PD) [8].

The etiology of FM remains unclear but is believed to result from complex interactions between genetic predispositions and triggering events like physical trauma, infections, and inflammatory joint diseases. Childhood traumatic experiences have also been considered potential factors in FM development, with a higher prevalence of adverse events reported among FM patients compared to healthy controls or individuals with other chronic pain conditions like RA. In light of these observations, our study aimed to compare major depression, panic and stress-related disorders, and life events between patients with primary FM (PFM) and those with FM secondary to RA (secondary fibromyalgia [SFM]).

Materials and Methods

This study was conducted at Birsa Munda Government Medical College and Hospital on OPD and IPD patients by Departments of Medicine, Orthopedics and Psychiatry collectively. In this cross-sectional observational study, a total of 45 patients diagnosed with PFM and 53 patients diagnosed with SFM were consecutively enrolled. The criteria for including patients with Fibromyalgia secondary to RA were as follows: (1) age ranging from 18 to 70 years; (2) confirmation of RA diagnosis based on the 2010 American College of Rheumatology (ACR) classification criteria [9], and FM diagnosis based on the 2016 ACR criteria [8] as determined by the involved physicians. Exclusion criteria for SFM patients comprised (1) severe and uncontrolled non-RA medical conditions; (2) neurological complications arising from RA or any other pre-existing neurological disorders; (3) ongoing major depressive episode or presence of moderate to severe depressive symptoms as indicated by a Zung self-rated depression scale score of ≥60 [10]; (4) alcohol/drug abuse or dependency; and (5) any clinical conditions that could potentially compromise the reliability of the evaluation. The inclusion criteria for PFM patients included (1) age within the range of 18 to 70 years and (2) confirmation of FM diagnosis based on the 2016 ACR diagnostic criteria [8]. Exclusion criteria for PFM patients were (1) inflammatory etiologies of pain; (2) severe and uncontrolled medical conditions; (3) history of neurological disorders; (4) ongoing major depressive episode or presence of moderate to severe depressive symptoms based on a Zung self-rated depression scale score of ≥60 [10]; (5) alcohol/drug abuse or dependency; and (6) any clinical conditions that could potentially affect the reliability of the assessment.

Lifetime diagnoses of Major Depressive Disorder (MDD), Panic Disorder (PD), and Post-Traumatic Stress Disorder (PTSD), which are among the most commonly reported psychiatric disorders in Fibromyalgia (FM) patients [11], were determined by an experienced psychiatrist using the Structured Clinical Interview for DSM-5 Axis I Disorders. Depressive symptoms were evaluated utilizing the Zung Self-rating Depression Scale [10], where a total score of less than 50 indicated an absence of depression, scores between 50 and 59 indicated mild depression, scores between 60 and 69 indicated moderate depression, and scores exceeding 70 indicated severe depression.

Stressful life events were assessed using the Paykel's Interview for recent life events [12]. This study specifically focused on recent negative life events, categorized into two groups: (a) non-physical events such as work-related issues, educational challenges, financial difficulties, bereavement, migration, courtship and cohabitation issues, legal matters, familial and social relationship problems, and marital issues; and (b) physical events related to personal health or physical condition/activity, such as clinically significant changes in weight or the forced cessation of physical activities. Pain levels were evaluated using a Visual Analog Scale (VAS) represented as a 10 cm line with markings from 0 to 10 at regular intervals, where 0 indicated no pain and 100 indicated the most severe pain. Participants were instructed to mark the line at the point corresponding to their perceived pain intensity. The Fibromyalgia Impact Questionnaire (FIQ [13]) is a 10-item scale designed to assess FM-related symptoms.

Results

In Table 1, there were no notable variations observed between the groups concerning their demographic, clinical, or disease severity parameters. However, patients with PFM exhibited significantly higher BMI values compared to the SFM group. Table 2 highlights that PFM patients had markedly higher rates of lifetime MDD and PD compared to the SFM patients. Conversely, there were no discernible differences between the groups regarding rates of PTSD. In Table 3, the majority of SFM patients reported that the only event occurring in the year leading up to FM onset was RA, whereas PFM patients predominantly cited non-physical events or reported no event at all. Logistic regression analyses, as detailed in Table 4, aimed to pinpoint factors significantly associated with PFM/SFM. The findings indicated that lifetime panic disorder and experiences of physical neglect were independent risk factors for PFM. While the model did not support the simultaneous inclusion of lifetime PD and MDD due to their correlation, the impact of PD appeared to be more pronounced.

Table 1: Clinico-demographic parameters in the study patients

Parameter	PFM patients	SFM patients	p-value
No. of patients	45	53	-
Gender, female n (%)	44 (97.78)	49 (92.45)	0.61
Age in years	51.5 ± 11.2	54.2 ± 8.9	0.18
Education In years	11.9 ± 3.4	10.2 ± 2.9	0.27
Marital status, n (%)			
Single	15 (33.33)	13 (24.53)	0.72
Married	22 (48.89)	31 (58.49)	
Divorced/widowed	8 (17.78)	9 (16.98)	
Occupation, n (%)			
Manager	5 (11.11)	8 (15.09)	0.84
White collar job	10 (22.22)	12 (22.64)	
Blue collar job	10 (22.22)	13 (24.53)	
Unemployed	20 (44.44)	20 (37.74)	
Age at onset of FM (years)	43.6 ± 11.8	46.2 ± 7.2	0.19
Duration of FM (years)	7.87 ± 7.3	7.45 ± 5.8	0.75
BMI	27.3 ± 4.1	28.2 ± 4.6	<0.05
ZSDS	39.42 ± 10.45	37.15 ± 8.97	0.65
Pain VAS	8.38 ± 1.45	7.98 ± 1.25	0.19

Table 2: Psychiatric disorders in FM patients

Parameter	PFM patients		SFM patients		p-value
	n	%	n	%	
Presence of lifetime MDD	35	77.78	21	39.62	<0.05
Presence of lifetime PD	23	51.11	8	15.09	<0.05
Presence of lifetime PTSD	9	20.00	12	22.64	0.91

Table 3: Recent Life Events in FM patients

Parameter	PFM patients		SFM patients		p-value
	n	%	n	%	
No	18	40.00	1	1.89	<0.05
Non-physical events	16	35.56	4	7.55	<0.05
Physical events	11	24.44	48	90.57	<0.05

Table 4: Factors independently associated with PFM or SFM (binary multivariate logistic regression)

Parameter	B	SE	Sig.
Lifetime panic disorder	1.79	0.61	<0.05
Physical neglect	1.66	0.75	<0.05
Constant	2.15	0.73	<0.05

Discussion

The results of our study highlight notable distinctions between patients with FM linked to RA and those with PFM concerning psychiatric comorbidities such as depression and anxiety, as well as predisposing and/or precipitating environmental factors. The prevalence of lifetime

MDD among PFM patients in our study falls within the upper range reported in existing literature (20%–80% [11]) and significantly differed from SFM patients (40%). Our findings align closely with those of [14], reporting a lifetime major depression rate of 62% in PFM patients compared to 27% in RA patients without SFM. The occurrence of lifetime PD was higher in PFM patients than in SFM patients and also higher than reported in some [15,16], but not all [17], previous studies. This variation could be attributed to our recruitment from a specialized tertiary care center, which tends to attract severe and complex cases. Logistic regression analysis indicated an independent association between lifetime PD and PFM. Wolfe et al. [18] investigated factors predicting FM development in RA patients, excluding those with FM and those with FMness scores exceeding 10 at baseline. Their study suggested that socio-demographic disadvantages, psychosocial distress, somatic comorbidities, severe RA, and severe FM symptoms increase the likelihood of FM development in RA patients. Overweight and obesity were linked to the future development of Secondary Fibromyalgia (SFM), as evidenced by higher BMI values in our SFM group, although it's noted that some SFM patients were under treatment with medications like methotrexate and corticosteroids, which can cause weight gain. The methodology for assessing depression in our study (diagnosis by a specialist after a structured psychiatric interview) differs significantly from that of Wolfe et al. (self-reported current depression with exclusion criteria for current depressive episodes and clinically significant depressive symptoms), making direct comparisons challenging. Our findings suggest that the differing prevalence of psychiatric comorbidities and environmental stressors may imply distinct pathogenetic pathways in PFM and SFM development, irrespective of the presence of primary medical conditions like RA. The overlap between FM and psychiatric disorders likely stems from shared biological and environmental factors, supporting the hypothesis that common genetic determinants affecting neurotransmitter, neurotrophic, and inflammatory systems interact with environmental stressors, predisposing individuals to both depression/anxiety and FM [19]. Thus, the pathogenetic pathway leading to PFM may involve interactions between genetic predisposition and environmental stressors, ultimately contributing to central nervous system dysfunction and the development of depression/anxiety.

Conclusion

Our study suggests that varying rates of psychiatric comorbidities and environmental adversities indicate distinct pathogenetic pathways in PFM and SFM, independent of primary medical conditions like RA. Evidence supports shared biological and environmental factors contributing to high comorbidity rates between FM and psychiatric disorders. This supports the hypothesis that genetic determinants affecting neurotransmitter, neurotrophic, and inflammatory systems, combined with environmental factors, predispose individuals to both depression/anxiety and FM development. Thus, interactions between genetic predisposition and environmental adversities likely lead to CNS dysfunction, contributing to depression/anxiety in PFM's pathogenetic pathway.

References

1. McWilliams DF, Walsh DA. Factors predicting pain and early discontinuation of tumour necrosis factor-α-inhibitors in people with rheumatoid arthritis: Results from the British Society for Rheumatology Biologics Register. BMC Musculoskelet Disord. 2016; 17:337.
2. Purabdollah M, Lakdizaji S, Rahmani A. Relationship between sleep, pain and inflammatory markers in patients with rheumatoid arthritis. J Caring Sci. 2017; 6:249-255.
3. Khan NA, Spencer HJ, Abda E, Aggarwal A, Alten R, Ancuta C, et al. Determinants of discordance in patients' and physicians' rating of rheumatoid arthritis disease activity. Arthritis Care Res. 2012; 64:206-214.
4. Lee YC. Effect and treatment of chronic pain in inflammatory arthritis. Curr Rheumatol Rep. 2013; 15:300.
5. Jones GT, Atzeni F, Beasley M, Fluss E, Sarzi-Puttini P, Macfarlane GJ. The prevalence of fibromyalgia in the general population: A comparison of the American College of Rheumatology 1990, 2010, and modified 2010 classification criteria. Arthritis Rheumatol. 2015; 67:568-575.
6. Lichtenstein A, Tiosano S, Amital H. The complexities of fibromyalgia and its comorbidities. Curr Opin Rheumatol. 2018; 30:94-100.
7. Wolfe F, Smythe HA, Yunus MB, Bennett RM, Bombardier C, Goldenberg DL, et al. The American college of rheumatology 1990 criteria for the classification of fibromyalgia. Report of the multicenter criteria committee. Arthritis Rheum. 1990; 33:160-172.
8. Wolfe F, Clauw DJ, Fitzcharles MA, Goldenberg DL, Häuser W, Katz RL, et al. Revisions to the 2010/2011 fibromyalgia diagnostic criteria. Semin Arthritis Rheum. 2016; 46:319-329.
9. Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham CO 3rd, et al. 2010 rheumatoid arthritis classification criteria: An American College of Rheumatology/European

league against rheumatism collaborative initiative. Arthritis Rheum. 2010; 62:2569-2581.
10. Zung WW. A self-rating depression scale. Arch Gen Psychiatry. 1965; 12:63-70.
11. Fietta P, Fietta P, Manganelli P. Fibromyalgia and psychiatric disorders. Acta Biomed. 2007; 78:88-95.
12. Paykel ES, Prusoff BA, Uhlenhuth EH. Scaling of life events. Arch Gen Psychiatry. 1971; 25:340-347.
13. Sarzi-Puttini P, Atzeni F, Fiorini T, Panni B, Randisi G, Turiel M, et al. Validation of an Italian version of the fibromyalgia impact questionnaire (FIQ-I). Clin Exp Rheumatol. 2003; 21:459-464.
14. Arnold LM, Hudson JI, Keck PE, Auchenbach MB, Javaras KN, Hess EV. Comorbidity of fibromyalgia and psychiatric disorders. J Clin Psychiatry. 2006; 67:1219-1225.
15. Epstein SA, Kay G, Clauw D, Heaton R, Klein D, Krupp L, et al. Psychiatric disorders in patients with fibromyalgia. A multicenter investigation. Psychosomatics. 1999; 40:57-63.
16. Malt EA, Berle JE, Olafsson S, Lund A, Ursin H. Fibromyalgia is associated with panic disorder and functional dyspepsia with mood disorders. A study of women with random sample population controls. J Psychosom Res. 2000; 49:285-289.
17. Alciati A, Caldirola D, Sarzi-Puttini P, Atzeni F, Grassi M, Perna G. Is panic disorder associated with clinical severity of fibromyalgia? A preliminary study in a tertiary-care centre. Clin Exp Rheumatol. 2016;34: S99-S105.
18. Wolfe F, Häuser W, Hassett AL, Katz RS, Walitt BT. The development of fibromyalgia I: Examination of rates and predictors in patients with rheumatoid arthritis (RA). Pain. 2011; 152:291-299.
19. Maletic V, Raison CL. Neurobiology of depression, fibromyalgia and neuropathic pain. Front Biosci. 2009; 14:5291-5338.