



## RISK OF FIBROMYALGIA IN RHEUMATOID ARTHRITIS PATIENTS IN TAIWAN: A NATIONWIDE POPULATION-BASED STUDY

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### ABSTRACT

**Background:** The burden of Fibromyalgia (FM) with rheumatoid arthritis (RA) is sufficient to warrant recognition as a high-priority disorder in governmental health strategies. However, the components of RA patients with FM have not been studied extensively in Taiwan. **Objective:** We investigated the incidence rates, risk factors, healthcare utilization, and comorbidities of FM with RA in Taiwan. **Methods:** The data enrolled in

the National Health Insurance Research Database from 1996 to 2010 were evaluated. The statistical methods included t test, ANOVA, and odds ratios with 95% confidence intervals (CIs).

**Results:** A total of 873 RA patients with FM were women (75.4%), a health service utilization rate of 98.1% for Western medicine, and both Western (rate of 1.9%) and Chinese medicines (rate of 1.5%). In all year and age groups, the health service utilization rates were significantly higher for females than males ( $p < 0.05$ ). The percentage rates were highest in people aged  $\geq 75$  years (25.7%). The affiliation-adjusted percentage rates were 34.2 in clinics and 31.4 in medical centers ( $p < 0.01$ ). The disorders of the muscle, ligament, and fascia of FM with RA-to-RA odds ratio was 21.43 (95% CI 2.88–159.46). **Conclusion:** The mean annual incidence was 7.16 per 100,000 person /year. The findings may serve as data for 98.1% of Western medicine utilization

among RA patients with FM, with peaks in the females, and clinics for treatment. Musculoskeletal disorder and anxiety were the most common comorbidities. Education program may help the RA patients with FM of life care.

**KEYWORDS:** rheumatoid arthritis, fibromyalgia, incidence, health service utilization, comorbidities.

## INTRODUCTION

Fibromyalgia (FM) is characterized by diffused widespread pain, multiple painful tender points, sleep disturbances, fatigue, cognitive alterations, headache, migraine, bowel habits, diffused abdominal pain, and urinary frequency. The key assessment domains of FM include pain, fatigue, disturbed sleep, altered physical and emotional functioning, and decreased patient global satisfaction and health-related quality of life.<sup>[1–12]</sup> Fibromyalgia (FM) may decrease in bone mineral density (BMD) because of decreased mobility. FM patients frequently suffer from high levels of disability.<sup>[13,14]</sup> Patients in FM with rheumatoid arthritis (RA) had a higher incidences of several comorbidities and greater emergency department (ED) utilization than those with RA. Annual expenditures were almost double in FM patients with rheumatoid arthritis (RA) (\$19395, SD= \$25440).<sup>[15]</sup>

In patients with rheumatoid arthritis (RA), concomitant FM has been reported in 14%–17% of the cases.<sup>[13,14]</sup> in Europe and the United States, the incidence of RA patients with FM were 2%–17.1%, and the overall incidence of FM was 1%–25.83%.<sup>[14–23]</sup> However, according to FM epidemiology, RA had high incidence in women.<sup>[2,4]</sup> FM was predominant in the female gender (75%–92.0%).<sup>[18, 22,24–29]</sup> In these studies, the age group with the highest incidences of FM was the 46–64 year-old group.<sup>[24–26,30]</sup>

The epidemiology of RA patients with FM has not been investigated well in Taiwan. To characterize comorbidities, 60%–70% of pain-related pharmacotherapy and healthcare resource were used among patients with FM (i.e., multiple drugs in clinical practice<sup>[5, 24–26]</sup>, physical therapy, exercise therapy, cognitive behavioral therapy, and supportive mental therapy).<sup>[31]</sup>

In Taiwan, in 2008, 22.89 million of the country's 22.96 million people (amounting to 99.7% of the island's population) were covered by the NHI program.<sup>[32]</sup> Most medical institutions (93%) have contracted NHI. The inhabitants of Taiwan are free to choose Western medicine

or traditional Chinese medicine and can choose to visit either public or private medical facilities. [33-35] Therefore, information from the NHI database is considered appropriate for the assessment of the epidemiological features of RA patients with FM in Taiwan. The aim of this study was to estimate the incidences of RA patients with FM in terms of sex, age, health service utilization, comorbidities and its related factors.

## MATERIALS AND METHODS

### Data collection

The Taiwanese NHI Bureau (NHIB) provided electronic data containing the patients' numbers, sex, date of birth, diagnostic codes, prescription drugs dispensed, medical cost, medical care facilities, and specialties. NHIB collects data from the NHI program and sorts them into data files per year. The data includes the registration files and original claims for reimbursement. These data files were de-identified by scrambling the identification codes of both patients and medical facilities, and the files were then sent to the National Health Research Institutes (NHRI) to from the original files of the NHI Research Database (NHIRD).

FM data with RA cases from 1996 to 2010 were collected from the Taiwanese NHIB, and 1,000,000 patients were used for this longitudinal study. The general population employed in this study included 215 men and 658 women. FM (with RA) cases from 1996 to 2010 were identified from the NHIRD by ICD-9-CM. The codes were converted into ICD-9-CM for data analysis. The average age-specific incidences during the target period were further compared and analyzed. Sex for specific periods (calendar year) were performed. RA (ICD-9-CM: 714.0) and FM (ICD-9-CM: 729.1) cases were explored in the contexts of traditional Chinese medicine, Western medicine resource utilization, and influencing factors. [7] The disease categories used to analyze comorbidities were osteoarthritis (715.90), anxiety (300.00), disorders of the muscle, ligament, and fascia (728.9), arthropathy (716.90), disorders of the muscle, ligament, and fascia (733.00), migraine (346.9), sicca syndrome (710.2), hereditary and idiopathic peripheral neuropathy (356.9), hypertension (401.9), disorder of the stomach (536.9), lumbago (724.2), and synovitis and tenosynovitis (727.00).

### Statistical analyses

The annual incidence refers to the number of new FM cases with RA divided by the size of the population at risk from 1996 to 2010. Percentage, t test, and ANOVA were used in the comparison of the differences in patients of Chinese medicine and Western medicine in terms

of medical resources in different circumstances and their utilization factors. The relative risks (RRs) and 95% confidence intervals (CIs) of FM cases with RA for comorbidities were associated with sex variables.  $p < 0.05$  was considered statistically significant.

### **Ethics**

All patients's data were all encrypted using the same encryption algorithm to cross-link the data while protecting the privacy of the patients. This study protocol was approved by the institutional review board (IRB) of China Medical University Hospital (CMUH103-REC1-088).

### **RESULTS**

Table 1 shows that during the 15-year period (1996 to 2010), the majority of cases involved men (24.6%,  $n = 215$ ) and 75.4% ( $n = 658$ ) involved women, the health service utilization rates were higher for females than males. The mean age of outpatient cases was 64.5 years, and the female-to-male ratio was 3.06. The  $\geq 75$  year-old group constituted 25.7% ( $n = 224$ ), and the 55–64 year-old group constituted 25.5% ( $n = 223$ ) of the total cases. The percentage rates were the highest among people aged  $\geq 75$  years old (25.7%) and lowest among people aged 0–14 years old (0.0%). The age-adjusted percentage rates were 30–39 years old, 40–54 years old, 55–64 years old, and 65–74 years old. The  $\geq 75$  year-old group had higher rates than the 15–29 year-old group ( $p < 0.05$ ). The affiliation-adjusted percentage rates were 34.2% in clinics and 31.4% in medical centers ( $p < 0.01$ ) (Table 1).

The annual number of RA patients with FM increased from the annual percentage of 1999 (4.2%) to 2001 (11.5%) and peaked in 2001 (11.5%). Our data also demonstrated that the maximum and minimum percentages of RA patients with FM occurred in 2001 (11.5%) and 1997 (0%), respectively. The 15–29 year-old group had the lowest percentage rate of 16 (1.8%), whereas the  $\geq 75$  year-old group had the highest at 224 (25.7%) (Table 2).

The annual incidence was 0.1–10.66 per 100,000 person/year (excluding 1997), and the mean annual incidence of IE was 7.16 per 100,000 person/year. The annual incidence of the maximum rate of RA patients with FM in 2000, 2001, and 2005 were 10.07, 10.66, and 10.26 per 100,000 person/years, respectively. The annual rate of RA patients with FM from 1999 to 2000, 2004, and 2007 to 2010 were significantly prevalent in females than in males (all  $p < 0.05$ ) (Table 3).

From 1996–2010, outpatient services used Western medicine at a rate of 98.1% (n = 856), followed by both services (traditional Chinese medicine and Western medicine) at a rate of 1.9% (n = 13) and traditional Chinese medicine services at a rate of 1.5% (n = 4). The annual number of Western medicine service utilization by RA patients with FM experienced an increase from 1998 (1.3%) to 2001 (11.2%), with a peak in 2005 (11.1%) (Table 4).

The comparison of subjects was randomly selected at a ratio of 5:1 relative to the population of RA patients and was matched by sex and age. The following are the comorbidities and possible causes of FM in RA patients among the 248 outpatients : osteoarthritis, 49 episodes (19.8%); anxiety, 26 episodes (10.5%); disorders of the muscle, ligament, and fascia, 24 episodes (9.7%); arthropathy, 23 episodes (9.3%); disorders of the muscle, ligament, and fascia, 21 episodes (8.5%); migraine, 18 episodes (7.3%); sicca syndrome, 18 episodes (7.3%); hereditary and idiopathic peripheral neuropathy, 17 episodes (7.1%); hypertension, 13 episodes (6.9%); disorder of the stomach, 13 episodes (6.9%); lumbago, 13 episodes (6.9%); synovitis and tenosynovitis, 13 episodes (6.9%). The comorbidities of the unspecified functional disorder of the stomach were higher for males than for females. The following are the comorbidities and possible causes of RA in patients among the 1295 outpatients: hypertension, 255 episodes (19.7%); osteoarthritis, 230 episodes (17.8%); sicca syndrome 225, episodes (17.4%); anxiety, 102 episodes (7.9%); arthropathy, 96 episodes (7.4%); hereditary and idiopathic peripheral neuropathy, 34 episodes (7.1%); lumbago, 80 episodes (6.2%); synovitis and tenosynovitis, 74 episodes (5.7%); disorders of the muscle, ligament, and fascia, 23 episodes (1.8%); migraine, 17 episodes (1.3%); disorders of the muscle, ligament, and fascia, 1 episode (0.1%)(Table 5).

Table 5 shows the comorbidities of osteoarthritis, anxiety, unspecified disorders of the muscle, ligament, and fascia, arthropathy, sicca syndrome, hereditary and idiopathic peripheral neuropathy, essential hypertension, unspecified functional disorder of the stomach, lumbago, synovitis and tenosynovitis. Unspecified comorbidities were significantly higher in RA patients with FM than in the RA patient group (all  $p < 0.05$ ). The rate of disorders of the muscle, ligament, and fascia of FM with RA-to-RA odds ratio were 21.43 (95% CI 2.88–159.46).

Table 1. Demographic characteristics of RA patients with FM, n = 873

Characteristics	Traditional Chinese medicine	Western medicine	Both of types of medicine	Total	t <sup>†</sup> or F <sup>†</sup> P value
	N (%)	N (%)	N (%)	N (%)	
<b>Sex</b>					
Female	11(84.6)	643(75.1)	4(100.0)	658(75.4)	1.9* 1 > 2
Male	2(15.4)	213(24.9)	0(0.0)	215(24.6)	
<b>Age</b>					
0–14	0(0.0)	0(0.0)	0(0.0)	0(0.0)	14.7* 3 > 2; 4 > 2; 5 > 2; 6 > 2; 7 > 2
15–29	1(7.7)	14(1.6)	1(25.0)	16(1.8)	
30–39	0(0.0)	39(4.6)	0(0.0)	39(4.5)	
40–54	1(7.7)	174(20.3)	0(0.0)	175(20.0)	
55–64	7(53.8)	213(24.9)	3(75.0)	223(25.5)	
65–74	3(23.1)	193(26.1)	0(0.0)	196(22.5)	
≥75	1(7.7)	223(26.1)	0(0.0)	224(25.7)	
<b>Type of affiliation</b>					
Medical center	7(53.8)	265(30.9)	2(50.0)	274(31.4)	4.8** 4 > 1
Regional hospital	5(38.5)	142(16.6)	1(25.0)	148(16.9)	
Local hospital	0(0.0)	152(17.8)	0(0.0)	152(17.4)	
Clinics	1(7.7)	297(34.7)	1(25.0)	299(34.2)	
Total	13(100.0)	856(100.0)	4(100.0)	873(100.0)	

\* $P < 0.05$  \*\* $P < 0.01$  \*\*\*  $P < 0.001$ 

† t or F data

Table 2. FM in RA patients in 1996–2010 by year and age group (n = 873)

Year/Age	0–14	15–29	30–39	40–54	55–64	65–74	≥75	Total
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
1996	0(0.0)	0(0.0)	0(0.00)	0(0.0)	0(0.00)	0(0.0)	1(0.1)	1(0.1)
1997	0(0.0)	0(0.0)	0(0.00)	0(0.00)	0(0.00)	0(0.0)	0(0.0)	0(0.0)
1998	0(0.0)	0(0.0)	0(0.00)	3(0.3)	0(0.00)	4(0.5)	4(0.5)	11(1.3)
1999	0(0.0)	0(0.0)	2(0.20)	7(0.8)	17(1.9)	6(0.7)	5(0.6)	37(4.2)
2000	0(0.0)	2(0.2)	5(0.8)	19(2.2)	17(1.9)	27(3.1)	25(2.9)	95(10.9)
2001	0(0.0)	1(0.1)	5(0.6)	13(1.5)	24(2.8)	16(1.8)	41(4.7)	100(11.5)
2002	0(0.0)	1(0.1)	1(0.1)	15(1.7)	17(1.9)	10(1.2)	23(2.6)	67(7.7)
2003	0(0.0)	1(0.1)	1(0.1)	19(2.2)	13(1.5)	16(1.8)	15(1.7)	65(7.5)
2004	0(0.0)	2(0.2)	3(0.3)	12(1.4)	17(1.9)	20(2.3)	15(1.7)	69(7.9)
2005	0(0.0)	3(0.3)	4(0.5)	16(1.8)	24(2.8)	22(2.5)	27(3.1)	96(11.0)
2006	0(0.0)	0(0.0)	3(0.3)	7(0.8)	19(2.2)	17(1.9)	25(2.9)	71(8.1)
2007	0(0.0)	3(0.3)	1(0.1)	15(1.7)	15(1.7)	16(1.8)	11(1.3)	61(6.9)
2008	0(0.0)	1(0.1)	5(0.6)	14(1.6)	18(2.1)	12(1.4)	14(1.6)	64(7.3)
2009	0(0.0)	0(0.0)	5(0.6)	15(1.7)	18(2.1)	12(1.4)	12(1.4)	62(7.1)
2010	0(0.0)	2(0.2)	4(0.5)	20(2.3)	24(2.8)	18(2.1)	6(0.7)	74(8.5)
Total	0(0.0)	16(1.8)	39(4.5)	175(20.1)	223(25.5)	196(22.5)	224(25.7)	873(100.0)

**Table 3. Annual incidence rate<sup>†</sup> of FM in RA patients in 1996–2010 by year and sex group (n = 873)**

Year/sex	Male N (%)	Female N (%)	Total N (%)	Incidence rate	t <sup>§</sup>
1996	0(0)	1(0.1)	1(0.1)	0.1	×
1997	0(0)	0(0)	0(0)	0	×
1998	2(0.2)	9(1.0)	11(1.3)	1.16	0.92
1999	7(0.8)	30(3.4)	37(4.2)	3.91	-4.03***
2000	27(3.1)	68(7.8)	95(10.9)	10.07	-4.04***
2001	26(2.9)	74(8.5)	100(11.5)	10.66	0.35
2002	18(2.1)	49(5.6)	67(7.7)	7.15	0.36
2003	11(1.3)	54(6.2)	65(7.5)	6.94	-0.14
2004	18(2.1)	51(5.8)	69(7.9)	7.37	-2.35*
2005	33(3.8)	63(7.2)	96(11)	10.26	-0.55
2006	12(1.4)	59(6.8)	71(8.1)	7.59	-0.45
2007	12(1.4)	49(5.6)	61(6.9)	6.52	2.74*
2008	22(2.5)	42(4.8)	64(7.3)	6.85	7.61***
2009	15(1.7)	47(5.4)	62(7.1)	6.63	5.48***
2010	12(1.4)	62(7.1)	74(8.5)	7.92	5.64***
Total <sup>‡</sup>	215(100)	658(100)	873(100)	7.16	5.16***

<sup>†</sup> Annual incidence (per 100,000 person/year) is the number of new cases of FM in RA patients divided by the size of the population at risk in each year.

<sup>‡</sup> The 15-year cumulative incidence is the number of new cases of FM in RA patients divided by the size of the population at risk from 1996 to 2010.

\* $P < 0.05$  \*\* $P < 0.01$  \*\*\* $P < 0.001$

<sup>§</sup> t data

**Table 4. Utilization of Western medicine and traditional Chinese medicine in RA patients with FM from 1996–2010**

Year	Subjects using Western medicines only N (%)	Subjects using traditional Chinese medicines only N (%)	Subjects using both of Western medicine and traditional Chinese medicine only N (%)
1996	1(0.1)	0(0.0)	0(0.0)
1997	0(0.0)	0(0.0)	0(0.0)
1998	11(1.3)	0(0.0)	0(0.0)
1999	37(4.3)	0(0.0)	0(0.0)
2000	94(10.9)	1(7.7)	0(0.0)
2001	96(11.2)	4(30.7)	0(0.0)
2002	64(7.5)	1(7.7)	2(50.0)
2003	64(7.5)	0(0.0)	1(25.0)
2004	68(7.9)	0(0.0)	1(25.0)

2005	95(11.1)	1(7.7)	0(0.0)
2006	69(8.1)	2(15.4)	0(0.0)
2007	61(7.1)	0(0.0)	0(0.0)
2008	62(7.2)	2(15.4)	0(0.0)
2009	60(7.0)	2(15.4)	0(0.0)
2010	74(8.6)	0(0.0)	0(0.0)
Total	856(100.0)	13(100.0)	4(100.0)

\*Health service utilization rate of 98.1%, 1.9%, and 1.5% for Western medicine, both Western and traditional Chinese medicine, and traditional Chinese medicine, respectively.

Denominator: 873

**Table 5. Comorbidities of RA patients with FM and RA patients in 1996-2010**

Rank	ICD-9 code*		Fibromyalgia in RA (N=248)			RA (N = 1295)			OR, 95%CI	P value
			Female N (%)	Male N (%)	Total N (%)	Female N (%)	Male N (%)	Total† N (%)		
1	715.90	Osteoarthritis	34(17.3)	15(2.9)	49(19.8)	180(16.9)	50(21.4)	230(17.8)	0.17 (0.12–0.24)	<0.001
2	300.00	Anxiety	24(12.2)	2(3.9)	26(10.5)	87(8.2)	15(6.4)	102(7.9)	0.24 (0.15–0.36)	<0.001
3	728.9	disorder of muscle, ligament, and fascia	18(9.1)	6(11.8)	24(9.7)	16(1.5)	7(2.9)	23(1.8)	1.04 (0.59–1.86)	<0.022
4	716.90	Arthropathy	16(8.1)	7(13.7)	23(9.3)	80(7.5)	16(6.8)	96(7.4)	0.22 (0.14–0.35)	<0.001
5	733.00	Unspecified disorder of muscle, ligament, and fascia	19(9.6)	2(3.9)	21(8.5)	1(0.1)	0(0)	1(0.1)	21.43 (2.88–159.46)	<0.001
6	346.9	Migraine	16(8.1)	2(3.9)	18(7.3)	15(1.4)	2(0.9)	17(1.3)	1.06 (0.54–2.07)	0.865
7	710.2	Sicca syndrome	16(8.1)	2(3.9)	18(7.3)	202(19.0)	23(9.8)	225(17.4)	0.06 (0.04–0.10)	<0.001
8	356.9	Hereditary and idiopathic peripheral neuropathy	14(7.1)	3(5.9)	17(7.1)	26(2.5)	8(3.4)	34(7.1)	0.49 (0.27–0.89)	<0.016
9	401.9	hypertension	12(6.1)	1(1.9)	13(6.9)	203(19.1)	52(22.2)	255(19.7)	0.04 (0.02–0.07)	<0.001
10	536.9	disorder of stomach	6(3.0)	7(13.7)	13(6.9)	122(11.5)	36(15.4)	158(12.2)	0.07 (0.04–0.12)	<0.001
11	724.2	Lumbago	10(5.1)	3(5.9)	13(6.9)	68(5.8)	12(5.1)	80(6.2)	0.15 (0.08–0.27)	<0.001
12	727.00	Synovitis and tenosynovitis	12(6.1)	1(1.9)	13(6.9)	61(6.4)	13(5.6)	74(5.7)	0.16 (0.09–0.30)	<0.001
Total			197(100.0)	51(100.0)	248(100.0)	1061(100.0)	234(100.0)	1295(100.0)	0.17 (0.15–0.20)	<0.001

\* ICD-9-CM was used to code and classify the morbidity data from the outpatient records.

† Total N (%): N, number of RA patients with FM with the percentages in parentheses.

## DISCUSSION

The present study is the first and largest 15 years population-based survey evaluating the incidences of RA patients with FM in Taiwan. the mean annual incidence of IE was 7.16 per 100,000 person/year. Our findings may serve as data for 98.1% of Western medicine utilization among RA patients with FM. The affiliation percentage rates were 34.2% in clinics. Osteoarthritis and anxiety were the most comorbidities that affected females and elderly patients with increasing trend <sup>[36]</sup>. Indeed, this study to obtain information that would be important for rheumatologists in planning education programs for Taiwan FM.

The 1990 ACR criteria defines FM as a history of chronic widespread pain, above and below the waist (including the whole length of the spine), and excessive bilateral tenderness when pressure is applied to 11 of 18 specific muscle-tendon sites. <sup>[10,22]</sup> The annual incidence of RA patients with FM increased from 2000 (10.07 per 100,000 person /year) to 2001 (10.66 per 100,000 person /year), with a peak in 2005 (10.26 per 100,000 person /year). Patients with physician-diagnosed fibromyalgia (prevalent cases) and applied modified American College of Rheumatology (ACR) 2010 research criteria to identify criteria-positive patients. <sup>[10]</sup> The incidence rates was 6.52-6.63 per 100,000 person /year from 2007 to 2009, 7.92 per 100,000 person /year in 2010. Our data also demonstrated that the annual incidence was 0.1–10.66 per 100,000 person /year in Taiwan. Mean annual incidence of RA patients with FM 7.16 per 100,000 person /year. The RA patients with FM incidence rate was reported at 0.5%–30.0% in various countries. <sup>[14, 16–17, 18–23,36]</sup> FM patients mainly go directly to rheumatology clinics to seek help. However, RA patients with FM patients still only account for 873 patients during the 15-year study period (1996–2010) in Taiwan rheumatology clinics. In Taiwan, few studies have been conducted on RA patients with FM in Taiwan. The lack of related research and the medium incidence of RA patients with FM in Taiwan indicate a potentially low awareness of FM by Taiwan hematologists.

Other studies show that 75%–92% of RA patients with FM were women. <sup>[18,22,24-26]</sup> In this study, the percentage rates in Taiwan were significantly higher among females than males. <sup>[2, 4, 27-29, 37-38]</sup> In this study, the age group with the highest incidences was  $\geq 65$  years old (48.2%). <sup>[24–26, 30,37]</sup> The apparent increasing trend in the annual percentage of RA patients with FM in Taiwan may be attributed to the aging population, which was inferred from the higher age of RA patients with FM. <sup>[27]</sup> Literature showed that high mortality was associated with FM, particularly in old patients and in subjects with comorbidities. <sup>[15, 20–21, 26–32, 37]</sup> The

results showed that subjects with prior hospitalizations had poor prognosis for osteoarthritis, disorders of the muscle, ligament, and fascia, and arthropathy. The RA patients with FM group had more severe pain, anxiety and depression. Fibromyalgia is associated with a higher level of perceived than is seen with RA. This difference appears to be associated with higher levels of pain condition by fibromyalgia patients.<sup>[38]</sup> However, the increasing trend in mortality can only partially be explained by the growing number of affected elderly patients. To correlate disease activity score (DAS-28) in the fibromyalgia patients with rheumatoid arthritis (RA), the average DAS score was high in fibromyalgia patients compared to those without fibromyalgia, RA patients with FM have more disability than those without FM.<sup>[22,38]</sup> FM has a significant impact on health status, social, emotional functioning, functional capacity, and quality of life.<sup>[9–12]</sup>

Outpatient services experienced Western medicine at a rate of 98.1%. The incidences of osteoarthritis, anxiety, and disorders of the muscle, ligament, and fascia were significantly higher in RA patients with FM than the RA patient group. The comorbidities of pain-related pharmacotherapy among patients with FM under multiple drugs had a rate of 60%–70% in clinical practice.<sup>[24–26]</sup> For pain-related beliefs, men were more likely to view pain as reflecting harm, and they were also more likely than women to use activity avoidance as a pain coping strategy.<sup>[39]</sup> The results of suggest that pain catastrophizing and fear of pain might increase the risk of developing multisite pain following musculoskeletal injury.<sup>[40]</sup>

The pharmacotherapy for FM has been most successful with central nervous system agents. Although these drugs carry labels such as antidepressants, muscle relaxants, or anticonvulsants, these drugs affect various neurochemicals that have a broad range of activities in spinal cord, including modulation of pain sensation.<sup>[41]</sup> Approximately 40%–50% of patients with FM multiple pharmacotherapy experienced musculoskeletal pain and chronic fatigue.<sup>[31, 34, 42]</sup> The percentage of study subjects receiving various pain-related medications increased. Among the RA patients with FM, 34.2% were affiliated with clinics. The chronic and plausible long-term disease explanations might be attributed to the substitution of ambulatory medicine for Western medicine services.

The comorbidities were osteoarthritis, disorders of the muscle, ligament, fascia, arthropathy, and back, which primarily affect neurophysiologic functions in a variety of combinations. To evaluate frequency of RA with FM patients and its effect on disease activity score.<sup>[5,37,43–46]</sup> This difference appears to be independent of levels of pain, depression and anxiety. 51.4% of

fibromyalgia patients and 14.8% with RA had fatigue, sleep or cognitive problems that were severe, continuous, and life-disturbing, and almost all fibromyalgia patients had severe impairments of function.<sup>[14,47]</sup> Manual therapy protocol was effective for improving pain intensity, widespread pressure pain sensitivity, impact of FMS symptoms, sleep quality, and depressive symptoms. In addition, sex differences were observed in response to treatment: women showed a greater reduction in pain and impact of FMS symptoms than men.<sup>[48]</sup> The Western medicine (female = 75.1%) and Traditional Chinese medicine (female= 84.6%) utilization rates were higher for females than males.

In conclusion, this study demonstrates that the mean annual incidence of RA patients with FM 7.16 per 100,000 person /year. In outpatient services used Western medicine at a rate of 98.1%. This study revealed a high incidence of RA with FM in women. Osteoarthritis, anxiety, and disorders of the muscle, ligament, and fascia were the most common comorbidities that affected elderly patients with increasing trend.

The use of the Health Insurance Database in this study presented some limitations. This database does not document lifestyle, and the lack of such valuable information hinders the evaluation of the respective influences of these factors.

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