



## NATIONWIDE POPULATION-BASED STUDY OF MEN WITH FIBROMYALGIA AND ASSOCIATE COMORBIDITIES IN TAIWAN

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Article Received on 07/07/2016

Article Revised on 28/07/2016

Article Accepted on 19/08/2016

### ABSTRACT

**Background:** We calculated the incidence rate of fibromyalgia (FM) and comorbidities because of the lack of previous studies based on the incidence data of FM in Taiwanese males. The study was a population-based retrospective cohort study. **Methods:** We analyzed the 2000–2009 claims data on outpatients for FM diagnosis (ICD-9-CM codes 729.1) from the National Health Insurance Research Database. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. **Results:** Cases of FM in 100,603 males (44.77%) and 125,632 females (55.53%) were studied, with a male to female ratio of 0.75–0.87. The annual incidences of men with FM from 2000 (20.57 per 1,000 people/year) to 2009 (18.62 per 1,000 people/year) and peaked in 2004 (25.40 per 1,000 people/year). Among the Taiwanese population, the incidence rate of men with FM was the highest data (115.21 per 1,000 people/year) than men from other countries. Comorbidities in men with FM include musculoskeletal pain conditions (36.10%), neuropathic pain conditions (14.64%), and respiratory tract infections (14.27%). The males of FM & non-FM related comorbidities showed significantly higher FM are of acute renal failure (OR 8.52, 95% CI, 1.05–69.47;  $p=0.045$ ), and hydronephrosis (OR 2.59, 95% CI, 0.88–7.65;  $p=0.085$ ). **Conclusion:** People with FM aged 40–64 years had a higher incidence and renal disease than the non-FM group. FM directly or indirectly interferes with or decreases the physical activity levels, emotional function and quality of life. Therefore, it is important to detect and treat FM early in order to promote physical activity and comorbidities control.

**KEYWORDS:** fibromyalgia, men, comorbidities, nationwide population-based study.

### INTRODUCTION

Fibromyalgia (FM) is a chronic disorder characterized by widespread musculoskeletal pain, tenderness, and fatigue, and often accompanied by sleep disturbance, depression, and anxiety. Numerous studies have indicated that the incidence rate of FM is related to age and sex. The incidence of FM has been reported in 1%–25.83%.<sup>[1–13]</sup> Fibromyalgia (FM) affects up to 6% of U.S. adults, resulting in a significant burden on the health care system and poor quality of life for patients.<sup>[14]</sup>

According to FM epidemiology, of those meeting the respective criteria sets, the ratio of females to males was 2.3–13.7:1.<sup>[3–4]</sup> The incidence rate of men FM was 7.0%.<sup>[15]</sup> In the general population, the prevalence of FM among men is 5–40 per 1,000 people/year.<sup>[16–19]</sup> Men with FM are at increased risk of reproductive problems, such as musculoskeletal pain conditions and renal disorders.<sup>[20–22]</sup>

In Taiwan, the National Health Insurance (NHI) program covers most of the population (the coverage rate in 2000 was 96.16%). Most medical institutions (93%) have contracted NHI, which is a large, stable national health

claims database. Likely, the majority of patients are seen by primary care physicians. The purpose of our study was threefold: 1. to determine the incidence of FM using a national database, 2. to evaluate the difference in incidence between males and females and age, and 3. to determine risk ratios for various comorbidities commonly associated with FM in men. Therefore, information from the NHI database is considered appropriate for assessing the epidemiological features of men with FM in Taiwan.

### MATERIALS AND METHODS

#### Data collection

The study was based on data from the National Health Insurance Research Database (NHIRD) in Taiwan. Through risk sharing, the public has received comprehensive medical care such as preventive medicine, clinical care, hospitalization, resident care, and social rehabilitation. In March 1995, the NHI service was initiated in Taiwan to provide comprehensive medical care to the public. According to the NHI annual statistics report, the coverage rate of NHI in 2007 was nearly 98.6% of the entire population of Taiwan, with more than 25 million people enrolled in the program. FM case

data from 2000 to 2009 were collected from the Taiwanese NHIB, and 1 million cases were used for this longitudinal study. The inclusion criteria were Discharge diagnosis (primary and first diagnosis) of this study included 100,603 men and 125,632 women. FM cases (ICD-9-CM: 729.1) from 2000 to 2009 were identified from the NHIRD by ICD-9-CM. Codes were converted into ICD-9-CM for data analysis. The average age-specific incidences during the target period were further compared and analyzed.

### Comorbidities

We analyzed comorbidities reportedly associated with FM, including musculoskeletal pain, neuropathic pain conditions, respiratory tract infections, gastrointestinal and liver disorders, cardiovascular disorders, mental disorders, sleep disturbances, dermatitis disorders, rheumatologic disorders, malignant diseases, renal and urinary disorders, metabolic disorders, genitor system, chronic fatigue syndrome, dementia disorders, other signs, symptoms, and ill-defined conditions. FM cases from 2000 to 2009 were identified from the NHIRD by ICD-9-CM. The codes were converted into ICD-9-CM for data analysis. The disease categories used to analyze comorbidities were arterial embolism and thrombosis of lower extremity (ICD-9-CM 444.22), other specified forms of chronic ischemic heart disease (ICD-9-CM 414.8), cerebral artery occlusion with cerebral infarction (ICD-9-CM 434.91), alcoholic liver damage (ICD-9-CM 571.3), chronic hepatitis (ICD-9-CM 571.40), acute renal failure, (ICD-9-CM 584.9), hydronephrosis (ICD-9-CM 591).

### Statistical analyses

The age- and sex-specific incidence rates were calculated by year using the NHIRD population. The annual incidence of FM and comorbidities, odds ratios (ORs), and 95% confidence intervals (CIs) were calculated. Annual incidence was calculated by dividing the number of new cases during a period by the number of individuals in the population at risk at the beginning of the study.  $p < 0.05$  was considered statistically significant.

### RESULTS

This study selected 226,235 individuals as subjects, consisting of 100,603 (44.47%) males and 125,632 (55.53%) females. The annual incidence was 19.96–

29.72 per 1,000 people/year, and the mean annual incidence of FM was 24.43 per 1,000 people/year (Table 1). Table 1 shows that the crude incidence rates of men with FM for each year were 20.57, 18.54, 25.20, 24.50, 25.40, 21.82, 19.39, 19.26, 18.10, and 18.62 people per 1,000 from 2000 to 2009, respectively. The annual incidences of men with FM increased from 2000 (20.57 per 1,000 people/year) to 2009 (18.62 per 1,000 people/year) and peaked in 2004 (25.40 per 1,000 people/year). The incidence rate in males compared with females was 115.21 versus 151.73 per 1,000 people/year. The ratio of males to females was 0.75–0.87:1 (Table 1). The 1–14 year –old of ratio of males to females was 1.27:1 (males: 5543; females: 4377) (OR 1.40, 95% CI, 1.00–1.97;  $p = 0.049$ ) (Table 2).

Table 2 shows that the male FM age group with the highest incidence was the 40–64-year-old group. The rates were highest among men aged 55–64 years (257.56 per 1,000 people/year) and aged 40–54 years (257.46 per 1,000 people/year), the lowest among men aged > 75 years.

We also examined the association between FM and the following comorbidities: musculoskeletal pain conditions (34.53%), neuropathic pain conditions (15.18%), respiratory tract infections (13.54%), gastrointestinal and liver disorders (13.52%), cardiovascular disorders (5.05%), mental disorders (4.22%), sleep disturbances (4.06%), dermatitis disorders (2.62%), other signs, symptoms, and ill-defined conditions (2.55%), renal and urinary disorders (1.57%), metabolic disorder (1.10%), genitor system (0.88%), rheumatologic disorders (0.49%), malignant disease (0.37%), chronic fatigue syndrome (0.28%), and dementia disorders (0.04%). The two most common comorbidities in men and women were musculoskeletal pain conditions and neuropathic pain conditions (Table 3).

In the comparison of FM comorbidities between males of FM & Non-FM are compared in Table 4. FM-related comorbidities, FM showed significantly higher FM are of acute renal failure (OR 8.52, 95% CI, 1.05–69.47;  $p = 0.045$ ), and hydronephrosis (OR 2.59, 95% CI, 0.88–7.65;  $p = 0.085$ ).

**Table 1. Annual incidence of fibromyalgia, 2000–2009**

Year	Annual incidence					
	Male	Female	Total	Male / Female ratio	OR (95% CI)	P value
2000	9,862 (20.57)	13,174 (28.44)	23,036 (24.43)	0.75:1	0.68 (0.360–1.31)	0.25
2001	8,832 (18.54)	11,451 (24.85)	20,283 (21.63)	0.77:1	0.70 (0.36–1.38)	0.30
2002	11,996 (25.20)	15,840 (34.40)	27,836 (29.72)	0.77:1	0.65 (0.35–1.19)	0.16
2003	11,654 (24.50)	14,937 (32.45)	26,591 (28.41)	0.78:1	0.71 (0.38–1.31)	0.27
2004	12,077 (25.40)	15,268 (33.18)	27,345 (29.22)	0.79:1	0.68 (0.37–1.25)	0.21
2005	10,373 (21.82)	12,618 (27.43)	22,991 (24.58)	0.82:1	0.41 (0.40–1.46)	0.76
2006	9,215 (19.39)	11,342 (24.66)	20,557 (21.98)	0.81:1	0.70 (0.36–1.38)	0.31

2007	9,153 (19.26)	10,797 (23.48)	19,950 (21.34)	0.85:1	0.79 (0.40–1.56)	0.79
2008	8,597 (18.10)	10,053 (21.87)	18,650 (19.96)	0.86:1	0.78 (0.39–1.56)	0.48
2009	8,844 (18.62)	10,152 (22.09)	18,996 (24.16)	0.87:1	0.83 (0.42–1.65)	0.60
<b>Total</b>	100,603 (115.21)	125,632 (151.73)	226,235 (132.98)	0.80:1	0.73 (0.56–0.95)	0.01

Annual incidence (per 1,000 people/year) is the number of new cases of fibromyalgia in patients divided by the size of the population at risk each year.

OR = odds ratio, CI = confidence interval

**Table 2. Average sex specific incidence of fibromyalgia, 2000–2009**

Age	Fibromyalgia			OR (95% CI)	P value
	Male	Female	Total		
1–14	5,543 (85.29)	4,377 (61.86)	9,920 (73.08)	1.40 (1.00–1.97)	0.049
15–29	23,882 (212.49)	26,944 (228.37)	50,826 (220.60)	0.91 (0.74–1.13)	0.40
30–39	19,003 (235.79)	23,331 (286.16)	42,334 (201.12)	0.77 (0.63–0.94)	0.01
40–54	28,005 (257.46)	40,156 (365.92)	68,161 (311.93)	0.60 (0.49v0.73)	<0.0001
55–64	10,457 (257.56)	14,930 (373.04)	25,387 (314.88)	0.58 (0.48–0.70)	<0.0001
65–74	5,360 (183.28)	5,544 (189.02)	10,904 (186.15)	0.96 (0.77–1.20)	0.73
≥75	8,353 (19.13)	10,350 (27.34)	18,703 (22.94)	0.69(0.39–1.26)	0.24

Annual incidence (per 1000 people/year) is the number of new cases of fibromyalgia in patients divided by the size of the population at risk each year.

OR = odds ratio, CI = confidence interval

**Table 3. Comorbidities system for fibromyalgia 2000–2009, by sex group**

System	Male (N)	%	Rank	Female (N)	%	Rank	Total (N)	%	Rank
Musculoskeletal pain conditions	15,290	36.10	1	21,238	33.49	1	36,528	34.53	1
Neuropathic pain conditions	6,200	14.64	2	9,859	15.55	2	16,059	15.18	2
Respiratory tract infections	6,042	14.27	3	8,277	13.05	4	14,319	13.54	3
Gastrointestinal and liver disorders	5,756	13.59	4	8,548	13.48	3	14,304	13.52	4
Cardiovascular disorders	2,323	5.48	5	3,014	4.75	5	5,337	5.05	5
Mental disorders	1,522	3.59	6	2,937	4.63	7	4,459	4.22	6
Sleep disturbances	1,343	3.17	7	2,954	4.66	6	4,297	4.06	7
Dermatitis disorders	1,118	2.64	8	1,656	2.61	8	2,774	2.62	8
Other Signs, symptoms, and ill-defined conditions	1,061	2.51	9	1,631	2.57	9	2,692	2.55	9
Renal and urinary disorders	730	1.72	10	934	1.47	10	1,664	1.57	10
Metabolic disorder	465	1.10	11	699	1.10	12	1,164	1.10	11
Genitor system	34	0.08	15	894	1.41	11	928	0.88	12
Rheumatologic disorders	159	0.38	13	359	0.57	13	518	0.49	13
Malignant disease	165	0.39	12	227	0.36	14	392	0.37	14
Chronic fatigue syndrome	131	0.31	14	165	0.26	15	296	0.28	15
Dementia disorders	15	0.04	16	25	0.04	16	40	0.04	16
<b>Total</b>	42,354			63,417			105,771		

Male Denominator (Number of occurrences): 100,603; Female Denominator (Number of occurrences): 125,632. musculoskeletal pain conditions including myalgia and myositis, lumbago, backache, fasciitis, sprains and strains, synovitis and tenosynovitis, pain in joint, cervicalgia, arthropathy, sprains and strains of lumbar, and pain in joint. neuropathic pain conditions including neuralgia, neuritis and radiculitis, sciatica, cervical root lesions, nerve root and plexus disorder, osteoarthritis, whether generalized or localized, lower leg, brachial neuritis or radiculitis, thoracic or lumbosacral neuritis or radiculitis, thoracic or lumbosacral neuritis or radiculitis. respiratory tract infections.

**Table 4. Comparison related comorbidities between men of fibromyalgia versus non-fibromyalgia**

System	Disease	ICD-9 code	Fibromyalgia	Non-fibromyalgia	OR (95% CI)	P value
			N	N		
Cardiovascular disorders	Arterial embolism and thrombosis of lower extremity	444.22	8	7	1.16 (0.40–3.32)	0.79
	Other specified forms of chronic ischemic heart disease	414.8	10	9	1.12 (0.44–2.89)	0.81
	Unspecified cerebral artery	434.91	13	11	1.21 (0.51–2.84)	0.66

	<b>occlusion with cerebral infarction</b>					
	<b>Total</b>		31	27	1.21 (0.66–2.24)	0.53
<b>Liver disorders</b>	<b>Alcoholic liver damage</b>	571.3	10	9	1.12(0.44–2.89)	0.81
	<b>Chronic hepatitis</b>	571.40	170	155	1.08 (0.85–1.36)	0.55
	<b>Total</b>		180	164	1.12(0.89–1.41)	0.34
<b>Renal disorders</b>	<b>Acute renal failure</b>	584.9	8	1	8.52 (1.05–69.47)	0.045
	<b>Hydronephrosis</b>	591	12	5	2.59 (0.88–7.65)	0.085
	<b>Total</b>		20	6	3.92 (1.50–10.23)	0.0053

Ninth revision of the *ICD-9-CM* (The International Classification of Diseases, Clinical Modification) was used to code and classify morbidity data from outpatient records.

OR = odds ratio, I = confidence interval

Fibromyalgia number: Non-fibromyalgia number ratio= 1:1

## DISCUSSION

The present study is the first population-based epidemiological study on men with FM in Taiwan. The findings data for the ratio of males to females were 0.75–0.87:1. The 1-14 year-old of ratio of males to females was 1.27:1 (males: 5543; females: 4377), males are more likely to be diagnosed with FM than females, Educational programs may be helpful for increasing knowledge of juvenile fibromyalgia.<sup>[3–14]</sup> Annual incidence rates were 18.62–25.40 per 1,000 people/year from 2000 to 2009. Among the Taiwanese population, the incidence rate of men with FM was the highest data (115.21 per 1,000 people/year) than men from other countries.<sup>[14–18]</sup> The renal disorders were the comorbidities that affected males and 40–64-year-old patients with an increasing trend, FM most often first occur in the middle adulthood age.<sup>[23]</sup>

To our knowledge, previous studies have not used nationwide insurance health data to investigate the incidence of men with FM; such data indicate a higher incidence of FM than those in most published studies. This study selected 226,235 individuals as subjects with 100,603 (incidence rate: 115.21 per 1,000 people/year) males and 125,632 (incidence rate: 151.73 per 1,000 people/year) females during the 10-year period.

In the present study, the age group with the highest incidence rate was  $\geq 40$ –64 years old.<sup>[24–30]</sup> The apparent increasing trend in the annual incidences of men with FM in Taiwan may be attributed to the aging population, which was inferred from the middle adulthood age of men with FM.<sup>[23]</sup> This study confirms the substantial comorbidities and medication burden among patients with FM, and suggests that this burden may be high in the middle adulthood individuals with this disease.

We also examined the first association FM of comorbidities was musculoskeletal pain conditions (34.53%) in Taiwan. 36.10% of musculoskeletal pain of FM in men. Fibromyalgia is a chronic disorder characterized by widespread musculoskeletal pain that reportedly affects 2% to 5% of the U.S. population.<sup>[31, 32]</sup> FM is a chronic disorder characterized by widespread musculoskeletal pain, tenderness, spondylosis / intervertebral disc disorders/other back problems.<sup>[1–13,16]</sup>

The spectrum of problems related to chronic pain was more severe in FM followed by CWP, strongly suggesting that these conditions should be diagnosed and adequately treated in individuals.

In the comparison of FM comorbidities between males of FM & Non-FM, FM showed significantly higher FM of renal disorders impact of symptoms, a higher prevalence of FM was found in hemodialysis patients than previously reported.<sup>[9–21]</sup> In relation to these, physical examination prevention programs may help reduce the risk of renal disorders.

In conclusion, this study demonstrates that the highest incidence of FM in men is found in the 40–64-year old age group.–The males of FM & Non-FM are related comorbidities showed significantly higher FM of acute renal failure. The large nationwide cohort represents the common phenotypes of FM comorbidities. FM directly or indirectly interferes with or decreases the physical activity levels and emotional function. Therefore, it is important to detect and treat FM early in order to promote physical activity and quality of life.

Our study has limitations. This database does not document job, family status and lifestyle. The lack of such valuable information makes it difficult to evaluate the respective influences of these factors.

## ACKNOWLEDGMENTS

This study was supported by the Central Taiwan University of Science (CTU105-P-05). This study was conducted partly by using data from the National Health Insurance Research Database provided by the Bureau of National Health Insurance and the Department of Health; this study was also managed by the National Health Research Institute. The interpretation and conclusions contained herein do not represent the opinions of the Bureau of National Health Insurance, the Department of Health, or the National Health Research Institute.

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