The Incidence of Fibromyalgia and Its Associated Comorbidities

A Population-Based Retrospective Cohort Study Based on International Classification of Diseases, 9th Revision Codes

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Background: The epidemiology of fibromyalgia is poorly defined. The incidence of fibromyalgia has not been determined using a large population base. Previous studies based on prevalence data demonstrated that females are 7 times more likely to have fibromyalgia than males and that the peak age for females is during the childbearing years.
Objective: We have calculated the incidence rate of fibromyalgia in a large, stable population and determined the strength of association between fibromyalgia and 7 comorbid conditions.
Methods: We conducted a retrospective cohort study of a large, stable health insurance claims database (62,000 nationwide enrollees per year). Claims from 1997 to 2002 were examined using the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes to identify fibromyalgia cases (ICD code 729.1) and 7 predetermined comorbid conditions.
Results: A total of 2595 incident cases of fibromyalgia were identified between 1997 and 2002. Age-adjusted incidence rates were 6.88 cases per 1000 person-years for males and 11.28 cases per 1000 person-years for females. Females were 1.64 times (95% confidence interval = 1.59–1.69) more likely than males to have fibromyalgia. Patients with fibromyalgia were 2.14 to 7.05 times more likely to have one or more of the following comorbid conditions: depression, anxiety, headache, irritable bowel syndrome, chronic fatigue syndrome, systemic lupus erythematosus, and rheumatoid arthritis.
Conclusion: Females are more likely to be diagnosed with fibromyalgia than males, although to a substantially smaller degree than previously reported, and there are strong associations for comorbid conditions that are commonly thought to be associated with fibromyalgia.

Key Words: fibromyalgia, incidence, epidemiology, comorbidity

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Fibromyalgia is a chronic disorder characterized by widespread musculoskeletal pain, sleep disturbance, and fatigue that reportedly affects 2% to 5% of the U.S. population.[1,2] Comorbid conditions such as psychiatric illnesses,[2] somatic disorders,[3–7] and autoimmune disorders[1,8–11] may coexist with this disease. Despite the high prevalence of fibromyalgia, little epidemiologic data have been published concerning its scope and magnitude. Few prevalence studies and only one incidence study exist. The prevalence studies to date have demonstrated that females are 7 times more likely to have fibromyalgia than males and that the peak age for females is during the "childbearing" years. Trends over time and causal factors are impossible to determine with prevalence data yet can be determined with incidence data.

We reported age- and sex-specific incidence rates for fibromyalgia using International Classification of Diseases, 9th Revision (ICD-9) codes from a large, stable national health claims database. Likely, a majority of patients were seen by primary care physicians. We also examined the association between fibromyalgia and the following comorbid conditions: psychiatric illnesses (depression and anxiety), somatic disorders (irritable bowel syndrome, headache, and chronic fatigue syndrome), and 2 autoimmune disorders (systemic lupus erythematosus and rheumatoid arthritis). We calculated risk ratios to estimate the magnitude of association between fibromyalgia and these comorbid conditions.

MATERIALS AND METHODS

Study Population

Cases of fibromyalgia were identified from 1997 to 2002 among insured members of the Deseret Mutual Benefits Administration (DMBA) database. The DMBA was established in 1970 to provide insurance to employees of the Church of Jesus Christ of Latter-Day Saints (commonly called Mormons or LDS) and their dependents. It is a nationwide insurance claims database with approximately 62,000 insured members per year. There are nearly equal numbers of men and women in the DMBA but substantially fewer members over age 65 as a result of Medicare eligibility. Because

TABLE 1. Number of People With Fibromyalgia in the Deseret Mutual Benefit Administration Database 1998–2002

Total number of new fibromyalgia cases	2595
Females	1689 (65%)
Males	906 (35%)
Stratified by number of visits over a 5-yr period (1998–2002)	
Patients with <5 visits	2218 (85.5%)
Patients with 5 or greater visits	377 (14.5%)

of competing insurance coverage and a likely substantial healthy worker effect among those over age 65, we eliminated them from further analyses. The database includes nationwide employees, although 68% reside in Utah. The annual turnover is less than 5%, thus providing an unusually stable population and health claims database for analyses.

Data Collection and Identification of Cases

We identified the insurance claims records from the DMBA for 1997 to 2002. We used International Classification of Disease, 9th Revision, Clinical Modification (ICD-9-CM) code 729.1 to identify fibromyalgia cases.[12] The ICD-9-CM code 729.1 is listed as "myalgias and myositis, unspecified" and includes the subheading "fibromyositis, NOS" (an outdated term now replaced by fibromyalgia). We then stratified the claims by calendar year, age (in 5-year intervals), and sex.

Comorbid Conditions

We analyzed 7 comorbid conditions reportedly associated with fibromyalgia: depression, anxiety, headache, irritable bowel syndrome, chronic fatigue syndrome, systemic lupus erythematosus, rheumatoid arthritis (see Table 3 for ICD-9 codes). We determined the prevalence of these conditions in patients diagnosed with fibromyalgia and in the general DMBA population for the years 1997 to 2002. We inspected the rates of the comorbid conditions and found them stable from year to year, so we aggregated the data to report a single prevalence rate for each comorbid condition.

Statistical Analyses

We calculated age- and sex-specific incidence rates by year using the 2000 U.S. standard million population for age adjustment. We then calculated risk ratios and 95% confidence intervals for 7 comorbid conditions.[13] Data were managed in Microsoft Access 2003 and Microsoft Excel 2002.

RESULTS

There were 10,824 visits for fibromyalgia between the years 1997 and 2002, representing 3506 patients. By excluding those seen with fibromyalgia in 1997, which more likely included prevalent cases, we found 2595 incident cases between the years 1998 to 2002 (Table 1). Of those, 65% of patients were female and 86% had fewer than 5 visits for fibromyalgia. Incidence rates are reported per 1000 person-years for age groups zero through 64 years in 5-year increments and by sex (Table 2). The incidence of fibromyalgia peaked at 12.66 per 1000 person-years (95% confidence interval [CI] = 10.44–14.87) for males and 20.86 cases per 1000 person-years (95% CI = 18.22–23.40) for females. The peak for both sexes occurred in the sixth decade of life (Fig. 1). The overall age-adjusted incidence rate was 6.88 cases per 1000 person-years for males and 11.28 cases per 1000 person-years for females. After adjusting for age, we found females 1.64 times (95% CI = 1.59–1.69) more likely than males to have fibromyalgia.

TABLE 2. Age- and Sex-Specific Incidence Rates for Fibromyalgia Among Patients Enrolled in the Deseret Mutual Benefit Administration Between 1998 and 2002

	Males			Females			
Age (years)	No.	Population	Incidence Rate* (95% CI)	No.	Population	Incidence Rate* (95% CI)	Rate Ratio
0–4	5	11,202	0.45 (0.06–0.84)	11	10,893	1.01 (0.41–1.61)	2.26 (0.79, 6.51)
5–9	14	13,748	1.02 (0.48–1.55)	18	13,129	1.37 (0.74–2.00)	1.35 (0.67, 2.71)
10–14	34	17,190	1.98 (1.31–2.64)	42	16,393	2.56 (1.79–3.34)	1.30 (0.82, 2.04)
15–19	81	23,008	3.52 (2.75–4.29)	130	20,889	6.22 (5.15–7.29)	1.77 (1.34. 2.33)
20–24	82	20,986	3.91 (3.06–4.75)	145	16,621	8.72 (7.30–10.14)	2.23 (1.70, 2.93)
25–29	38	6578	5.78 (3.94–7.61)	82	7601	10.79 (8.45–13.12)	1.87 (1.27, 2.74)
30–34	44	5365	8.20 (5.78–10.62)	86	6404	13.43 (10.59–16.27)	1.64 (1.14, 2.35)
35–39	58	6736	8.61 (6.39–10.83)	100	7858	12.73 (10.23–15.22)	1.48 (1.07, 2.04)
40–44	98	8335	11.76 (9.03–14.09)	154	10,435	14.76 (12.43–17.09)	1.26 (0.97, 1.62)
45–49	118	10,203	11.57 (9.48–13.65)	243	11,932	20.37 (17.80–22.93)	1.76 (1.41, 2.19)
50–54	125	9877	12.66 (10.44–14.87)	249	11,965	20.81 (18.23–23.40)	1.64 (1.34, 2.04)
55–59	112	9726	11.52 (9.38–13.65)	240	11,506	20.86 (18.22–23.40)	1.81 (1.45, 2.27)
60–64	97	8390	11.56 (9.26–13.86)	189	9196	20.55 (17.62–23.48)	1.78 (1.39, 2.27)
Total	906	151,344	5.99 (5.60–6.38)	1689	154,822	10.91 (10.39–11.43)	1.82 (1.68, 1.97)
Adjusted for age†			6.88 (6.71, 7.05)			11.28 (11.06–11.50)	1.64 (1.59–1.69)

*Incidence rate per 1000 person-years.
†Age-adjusted using 2000 U.S. standard million population.
CI indicates confidence interval.

TABLE 3. Associations of Comorbid Conditions Among Patients Diagnosed With Fibromyalgia in the Deseret Mutual Benefit Administration Database Between 1998 and 2002

	Depression	Anxiety	Headache	IBS	CFS	SLE	RA
Females							
Patients with fibromyalgia = 1689	128	373	1080	219	70	42	103
Patients without fibromyalgia = 52,698	1401	3350	9307	1535	387	227	722
Risk ratio (95% CI)	2.85 (2.38–3.42)	3.47 (3.12–3.87)	3.62 (3.40–3.86)	4.45 (3.86–5.13)	5.64 (4.38–7.28)	5.77 (4.15–8.02)	4.45 (3.62–5.47)
Males							
Patients with fibromyalgia = 906	44	142	343	51	21	1	32
Patients without fibromyalgia = 52,323	873	2288	5123	743	172	27	303
Risk ratio (95% CI)	2.91 (2.15–3.94)	3.58 (3.03–4.25)	3.87 (3.47–4.31)	3.96 (2.98–5.26)	7.05 (4.48–11.09)	2.14 (0.29–15.74)	6.10 (4.24–8.78)

Depression includes single episode of major depressive disorder (MDD) and recurrent MDD (ICD-9-CM 296.2 and 296.3).
Anxiety includes generalized anxiety disorder, panic disorder, anxiety state unspecified (ICD-9-CM 300.00, 300.01, and 300.02).
Headache includes headache, tension headache, classical migraine, common migraine, variants of migraine, other forms of migraine, migraine unspecified (ICD-9-CM 307.81, 346.0, 346.1, 346.2, 346.8, 346.9, and 784.0).
IBS indicates irritable bowel syndrome (ICD-9-CM 564.1); CFS, chronic fatigue syndrome (ICD-9-CM 780.71); SLE, systemic lupus erythematosus (ICD-9-CM 710.0); RA, rheumatoid arthritis (ICD-9-CM 714.0); CI, confidence interval; ICD-9-CM, International Classification of Diseases, 9th Revision, Clinical Modification.

We identified 335 cases of fibromyalgia in patients under the age of 20. Rates rose with age. Female enrollees aged 15 to 19 had the highest incidence (6.22 per 1000 person-years [95% CI = 5.15–7.29]). This population mirrored the adult population in that female patients were more likely to be diagnosed with fibromyalgia than males of the same age.

Patients with fibromyalgia were more likely to be diagnosed with one or more of 7 predetermined comorbid conditions (Table 3). Of the psychiatric diagnoses, males and females with fibromyalgia were 2.9 to 3.6 times more likely to have a diagnosis of depression or anxiety. Those with fibromyalgia were 3.6 to 7.0 times more likely to be diagnosed with headache, irritable bowel syndrome, or chronic fatigue syndrome. For the autoimmune diseases, males and females with fibromyalgia were 2.1 to 6.1 times more likely to have rheumatoid arthritis or systemic lupus erythematosus.

DISCUSSION

The purpose of our study was 3-fold: 1) to determine the incidence of fibromyalgia using a national database and ICD-9 codes, 2) to evaluate the difference in incidence between females and males, and 3) to determine risk ratios for various comorbid conditions commonly associated with patients with fibromyalgia.

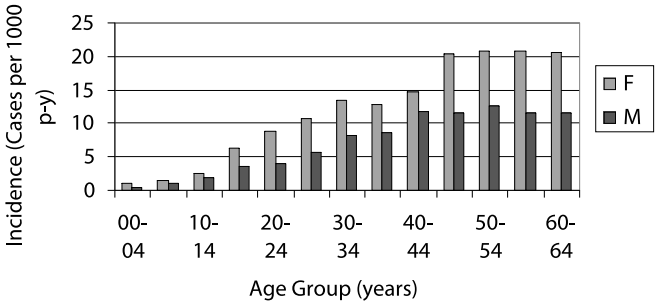

FIGURE 1. Age- and sex-specific incidence rates of fibromyalgia in the DMBA population 1998–2002.

Existing Epidemiology

Epidemiologic data on fibromyalgia are scant. The only previously published incidence study was based on 12 cases. They reported an incidence of 5.83 cases per 1000 person-years for 20- to 49-year-old women.[14] In our study, women aged 20 to 49 (n = 810) had an incidence rate of 13.31 cases per 1000 person-years (see Table 2).

Another study reported that women are 7 times more likely than men to have fibromyalgia.[2] That study identified subjects by using community-wide questionnaires followed by a physical examination. Mailed questionnaires are likely to contain significant selection biases and could account for the larger magnitude of sex difference previously reported. We found a more modest difference (relative risk = 1.64).

Comorbid Conditions

The relationship between fibromyalgia and comorbid illnesses has been suggested by previous authors.[1–11] We found patients with fibromyalgia were 2 to 7 times more likely than patients without fibromyalgia to have been diagnosed with one of the following 7 comorbid conditions: depression, anxiety, headache, irritable bowel syndrome, chronic fatigue syndrome, systemic lupus erythematosus, and rheumatoid arthritis.

The reported prevalence of fibromyalgia in patients with established comorbid conditions varies widely (Table 4).[1,3–11] For example, in patients with systemic lupus erythematosus, the prevalence of fibromyalgia ranged from 1% to 65%.[8,9] The small number of cases (10–18 per study) likely created substantial instability in those estimates. Additionally, prevalence, not risk ratios, was determined. We had 42 female cases and a large control group, enabling us to calculate a more stable risk ratio. Our calculated risk ratio for women who had fibromyalgia and systemic lupus erythematosus was 5.77 (95% CI = 4.15–8.02).

TABLE 4. Literature Review: Prevalence and Odds Ratios of Fibromyalgia With Comorbid Conditions

Comorbid Condition	Author	Prevalence of Fibromyalgia	Odds Ratio of Fibromyalgia
Depression	Wolfe et al[2]		4.22
Anxiety	Wolfe et al[2]		4.89
Irritable bowel syndrome	Sperber et al,[3] Whitehead et al,[4] Aaron et al[5]	32%, 49%, 77% (lifetime prevalence)	
Migraine headache	Peres et al[6]	35%	
Chronic fatigue syndrome	Aaron et al[5]	70% (twin study)	>20 (twin study)
Systemic lupus erythematosus	Ostuni et al[8]	1%	
	Valencia-Flores et al,[9]	10%	
	Grafe et al[10]	30%	
	Neumann, Buskila[1]	65%	
Rheumatoid arthritis	Wolfe, Michaud[11]	17%	

Our risk ratios for patients with fibromyalgia and either depression or anxiety are less than the only odds ratios reported in the literature. In that study, the odds ratios for patients with fibromyalgia who had depression or anxiety were 4.22 and 4.89, respectively.[2] We found the risk ratio between fibromyalgia and depression to be 2.91 for males and 2.85 for females. The risk ratios for those who had fibromyalgia and anxiety were 3.58 for males and 3.47 for females.

Strengths

Our study is a population-based retrospective cohort of employed individuals and their families seen in a large number of clinics, and therefore likely subject to a minimal amount of selection bias for or against the development of fibromyalgia or any other illness. The findings from this study are likely generalizable to most patients seen in the outpatient setting.

The DMBA database represents a population of approximately 62,000 with little annual turnover. There is also a financial incentive to code properly because improperly coded claims will delay reimbursement for services. Although errors in coding may occur, they are believed to be infrequent and nondifferentially distributed among those with and without fibromyalgia.

Biases/Limitations

Diagnostic accuracy is a concern with a study using a claims database. We used ICD-9-CM code 729.1 as a way of identifying patients with fibromyalgia. Although we were unable to determine if a patient was seen by a rheumatologist, likely a majority of patients were diagnosed with fibromyalgia by primary care physicians. Because we were unable to review patient charts, is possible that we have selected patients who were not intended to be diagnosed as having fibromyalgia (miscoding) or would not meet the diagnostic criteria established for research purposes by the American College of Rheumatology (misdiagnosis).[15]

Despite not being able to review charts, there are data that demonstrate the accuracy of the ICD-9 codes in the DMBA database. First, we compared our prevalence rates for fibromyalgia with the previously published rates. Wolfe et al reported a prevalence of 2%.[2] We found a prevalence of 1% (data not shown), suggesting that we did not include a large number of patients who did not have fibromyalgia.

Second, unpublished data from the DMBA database have demonstrated consistency when compared with national data (Drake HL, Shen S, Osmond GW, et al. Inpatient hospitalization rates among a non-smoking, non-drinking population, unpublished data). Hospital discharge rates from the DMBA database and the Nationwide Inpatient Sample (NIS) for the year 2002 were similar (rate ratio = 1.11, 95% CI = 1.10–1.12). There was also no statistical difference between the reason for hospitalization in the DMBA and NIS data for a number of disease categories, including "diseases of musculoskeletal system and connective tissue."

Lastly, we determined risk ratios (RRs) for diseases that would not likely be associated with fibromyalgia to serve as a control for the comorbid conditions associated with fibromyalgia (Table 3). After adjusting for age, we determined the following risk ratios among patients with fibromyalgia (data not shown): diabetes (RR = 1.42, 95% CI = 1.32–1.53), anemia (RR = 0.55, 95% CI = 0.40–0.70), and disorders of refraction/accommodation (RR = 1.11, 95% CI = 0.99–1.23). The risk ratio for patients with fibromyalgia and diabetes may be elevated because both have been shown to be associated with physical inactivity.[16,17]

Another limitation of the DMBA database is that it includes only 2 diagnoses per visit. It is possible, for example, that a physician seeing a patient with fibromyalgia and other medical problems might not include fibromyalgia as one of the patient's top 2 ICD-9-CM codes at any point in treatment. Likely, the use of ICD-9-CM diagnosis code 729.1 is not overstating the number of patients diagnosed with fibromyalgia.

Another potential limitation was the possibility that patients diagnosed with fibromyalgia might have more frequent clinic visits and therefore accumulate more comorbid diagnoses than a patient who is seen less frequently. We found that 85% of our fibromyalgia cases had been seen less than 5 times in 5 years, demonstrating that this effect appears to have been minimal (Table 1).

This study involved a stable population who had at least one family member employed and covered under the insurance plan. Therefore, it is possible that the study results are not generalizable to those whose family is entirely unemployed, migratory workers, or those who rely on traditional care for the uninsured (eg, university and county/public hospitals).

Significance

We calculated the first incidence rate of fibromyalgia in a large population-based setting. We also confirmed the belief that females are more likely to be affected than males, although to a substantially smaller degree than previously reported. Confirmation with future population-based studies of a more modest sex difference would argue that fibromyalgia should be considered more frequently in men.

We found strong associations for comorbid conditions that are commonly thought to be associated with fibromyalgia. Awareness of these associations may prompt both primary care clinicians and rheumatologists to address comorbid conditions when dealing with patients with fibromyalgia. These elevated risk ratios suggest that fibromyalgia and comorbid conditions may share a common etiology as previously suggested by other authors.[18–21] Future cohort studies over longer time periods could address the issue of whether fibromyalgia is diagnosed before or after comorbid conditions are established.

Clinical rheumatologists may find our data helpful in that it reflects how primary care physicians are diagnosing fibromyalgia. Because primary care physicians are seeing the majority of patients with fibromyalgia,[22] trends in their diagnosing patterns may affect the type of patients (and associated comorbid conditions) that are being referred to rheumatologists.

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