Utilization of Healthcare Services and Drug Consumption in Fibromyalgia: A Cross-Sectional Analysis of the Clalit Health Service Database

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Abstract

Aim: To investigate the health care utilization and drug consumption of patients with fibromyalgia (FM).

Materials and Methods: This is a cross-sectional study using the Clalit Health Care database. Clalit is the largest HMO in Israel, serving more than 4.4 million enrollees. We identified FM patients and age and sex-matched controls. Indicators of healthcare utilization and drug consumption were extracted and analyzed for both groups.

Results: The study included 14,296 FM patients and 71,324 controls. The mean age was 56 years, with a female predominance of 92%. Utilization rates across all healthcare services were significantly higher among FM patients, including rheumatology (OR 11.36, P<0.001), pain (36.8, P<0.001) and general practitioner clinics (OR 3.82, P<0.001), as well as emergency room visits (2.39, P<0.001) and hospitalizations in internal medicine wards (1.57, p<0.001). Drug use was significantly and consistently higher among FM patients compared to controls; NSAIDs (non-steroidal anti-inflammatory drugs) OR 2.56, P<0.001; opioids OR 4.23, P<0.001; TCA (tricyclic antidepressants) OR 8.21, P<0.001; anticonvulsants OR 6.31, P<0.001; SSRI (selective serotonin reuptake inhibitors) OR 2.07, P<0.001; SNRI (serotonin-norepinephrine reuptake inhibitor) OR 7.43, P<0.001.

Conclusion: Healthcare utilization and drug use are substantially higher among patients with fibromyalgia compared to controls

Introduction:

Fibromyalgia (FM) is a chronic pain disorder characterized by the presence of widespread debilitating pain. Other common associated symptoms include fatigue, unrefreshing sleep, cognitive impairment, mood disorders, and other psychiatric conditions The presenting symptoms are often ambiguous and non-specific and may overlap with other rheumatic conditions [1]. Since the diagnosis is solely reliant on subjective criteria, without objective laboratory or imaging tests to support the diagnosis, physicians often face uncertainty in establishing the diagnosis of FM, which leads to unnecessary and often costly diagnostic testing and treatment deferrals [2, 3].

The characteristics of FM bring about excessive use of medical resources in order to try to establish a "proper" alternative diagnosis [3]. According to a study by Berger et al. [4], physician office and emergency room visits, as well as prescription of pain-related medications, were four times higher in patients with FM compared to controls. In addition, medications are rapidly stopped by FM patients due to presumed intolerance or lack of efficacy, leading to low levels of adherence and an endless pursuit of a "wonder medication" that will solve all the

patients' ails [5]. Several studies suggest that this excessive use of health care services does not decline following the diagnosis of FM but rather continues along with the illness [6, 7].

The profuse healthcare utilization results in a substantial economic burden on the healthcare system. This burden is substantial when considering that FM patients have been shown to consume more healthcare resources than age and sex-matched controls without FM and also for those with chronic debilitating inflammatory disorders and other serious pain disorders [8–10].

This study aimed to examine the pattern of healthcare utilization amongst FM patients in comparison with healthy controls in Israel. The information was obtained by analyzing data recorded in the Clalit Health Services (CHS) database. CHS is the largest medical care provider in Israel and provides health care services for more than 4,400,000 people.

Methods

The Institutional Review Board of the CHS general management approved the study and exempted from the need to sign an informed consent form. The Declaration of Helsinki protocols were followed.

This study is one of a series of explorative and analytic studies based on the chronic disease registry of CHS, the largest healthcare provider in Israel. CHS is an integrated health maintenance organization (HMO) service in Israel which provides healthcare to more than 4,400,000 insured enrollees (>50% of the Israeli population). The CHS central computerized database was founded in 1998 and since collects medical and administrative data originating from its healthcare facilities. The registry is subjected to a continuous validation process based on repeated appraisals of diagnoses made by CHS physicians, registered prescriptions, pharmacy

claims, laboratory tests, and auxiliary tests for each patient. Comparison between diagnoses, drug administration, and laboratory and auxiliary tests from various sources is performed regularly, and inconsistencies are addressed and resolved after authentication by the registry manager. The data in the digitalized medical records undergo a series of verification. The validity of the data was found to be of high quality, as shown in previous studies [11–13].

Subjects

Our study was designed as a cross-sectional study with age and sex-matched controls. The FM group consisted of patients with at least one documented diagnosis of FM in their medical records between 1998 and 2016, registered by a CHS physician (as outpatients) or according to hospital discharge letters (as inpatients). The controls were age- and sex-matched patients without a mentioned diagnosis of FM drawn from the general population of CHS who enrolled during the same period as their match. The database was searched for patients with a diagnosis of FM registered between 1998 and 2016. The healthcare resource cost was compared for FM and control patients from the beginning of January 2014 until the end of December 2014.

The extracted information included: sex, age, smoking status, socioeconomic

status (on a scale of "low-medium-high"), weight, and Body-Mass Index (BMI). All of the parameters were well-validated in previous studies [14, 15]. Drug consumption data were extracted from pharmacy claims.

Statistical Analysis

Statistical analysis was performed using the R Statistical Software (version 3.2.2; R Foundation for Statistical Computing, Vienna, Austria). Comparative analysis of data was performed; continuous variables were compared using t-tests, and categorical variables were compared using the chi-square test. The association between FM patients and healthcare services utilization burden and drug consumption was tested by univariate analysis and by the multivariate logistic regression model. To further evaluate the relationship between FM and health services use, the number of visits to the primary care physician, emergency department and hospital admissions were stratified into two groups: regular and high-frequency users. High users were defined as subjects that addressed these services at rates higher than the 97.7% percentile of the non-FM control cohort. The percentage of the FM cohort and non-FM cohort who visited a pain management clinic or rheumatology clinic were compared as well. A multivariate logistical regression model was applied for each of the above-mentioned health services standardized for sex, age and SES. A p-value <0.05 was considered statistically significant.

Results

Overall, 14,269 fibromyalgia patients and 71,324 age and sex-matched controls were included in the study. The majority were female (92%) with an average age of 55 years. A higher proportion of FM patients were smokers (32.7% vs. 28%, $p<0.001$) and of lower SES (46.8% vs. 39%, $p<0.001$) compared to controls (Table 1).

The odds ratio (OR) for the use of every medication group analyzed were significantly higher among FM patients compared with controls: NSAID (non-steroidal anti-inflammatory drugs): OR 2.56, $P<0.001$; opioids: OR 4.23, $P<0.001$; TCA (tricyclic antidepressants): OR 8.21,

P<0.001; anticonvulsants: OR 6.31, P<0.001; SSRI (selective serotonin reuptake inhibitors): OR 2.07, P<0.001); SNRI (serotonin-norepinephrine reuptake inhibitor): OR 7.43, P<0.001 (Table 2).

In logistic regression models standardized for sex, age and socio-economic status the utilization of all community services was significantly higher in the FM group (Table 3): general practitioner visits (OR, p<0.001), rheumatology clinics (OR, p<0.001), pain clinics (OR 36.8, p<0.001) and hospital health care services, including admissions to internal medicine wards (OR1.57, p<0.001) and emergency room visits (2.39, p<0.001).

Discussion:

Our study identified significantly higher health care utilization among FM patients in comparison with non-FM subjects. All of the examined medications and medical services were consumed in higher proportions by FM patients compared to non-FM controls. These findings are consistent with findings in previous studies [16–19].

Female preponderance was observed in our cohort, reflecting similar trends from other epidemiological studies on FM [20]. Female patients have been shown to utilize healthcare services more than male patients [21] even after controlling for health status and socio-economic status[22].

The diagnosis of FM is often obscure and challenging. Symptoms are heterogeneous and interchangeable with other disorders, which complicate the arrival of the diagnosis [23]. According to the 2016 Revisions to the 2010/2011 Fibromyalgia Diagnostic Criteria [24], the syndrome is not a diagnosis of exclusion and does not exclude the presence of other concomitant

illnesses. Work-up should be directed to exclude the underlying etiologies. Therefore, physicians need to utilize the full range of diagnostic imaging, laboratory tests, and medical consultants in the course of diagnosis subsequently increasing health care utilization and costs. However, after reaching a diagnosis, the medical approach should, of course, be aimed at limiting frivolous health care costs, an aim that is often not achieved. At the same time, some physicians are doubtful regarding the existence of FM [25] which in turn promotes further utilization of health care resources.

The proportion of visits to rheumatologists were higher than for primary care and pain physicians. This suggests that despite FM requiring a multi-disciplinary approach, rheumatologists continue to play a central role in its diagnosis and treatment [26]. Another reason that rheumatology visits may account for a high percentage of clinic visits amongst FM patients in our study may reflect the concurrence of FM with other rheumatologic conditions [27, 28]

Previous studies have also reported higher levels of comorbidities among FM patients compared to healthy controls. Common concurrent diagnoses include tension headaches, migraine headaches, interstitial cystitis, irritable bowel syndrome, and chronic prostatitis [21, 29, 30] Patients with FM are also at an increased risk of coronary heart disease [31], heart failure [32], and inflammatory bowel disease [33]. In addition, 30% of FM patients had been subjected to a traumatic stressor such as trauma, surgery, or motor vehicle accidents.

The burden of somatic diseases among FM patients results in increased use of medical resources. Furthermore, the mounting comorbidities in FM are likely to mask the genuine inherent clinical

manifestation of FM itself. This often leads to a lack of successful treatment and potential dangerous overtreatment of associated comorbid conditions [34].

Treatment of fibromyalgia is complex and relies on both pharmacological and non-pharmacologic therapy. There are conflicting results regarding the effectiveness of pharmacologic treatment in FM [35–37].

A Multi-disciplinary approach, using combined treatment approaches is carried out in the management of FM. Different medications have shown to grant positive effects across different clinical domains in fibromyalgia, including pain relief, depression, and improving quality of life [38–40], yet, the approved medications for FM provide only marginal relief, and extensive treatment gaps remain across most clinical aspects of the syndrome. Two comprehensive Cochrane reviews found that the TCA amitriptyline provided sufficient pain relief in only 25% of patients [41] and that the anticonvulsant pregabalin produced a 30% reduction in pain scores in only 10% of FM patients [42]. A large population-based study by Kim et al. [43], utilizing commercial insurance claims data reported high health care utilization among FM patients before and after initiation of amitriptyline, duloxetine, gabapentin, or pregabalin, further highlighting the limited efficacy of current recommended medical solution in fibromyalgia. According to a Cochrane review, combination pharmacotherapy to overcome these unmet needs does not seem to provide established benefit [44] and at the same time resulted in high health care expenditure [45].

Opioids were heavily utilized in our cohort despite their limited value [2]. This is surprising given their deleterious impact on both health and psychosocial status among patients with FM and considering many recommendations against their use by many medical associations [36]. We

speculate that the extensive opioids usage in our cohort paradoxically promoted further healthcare consumption[46]

Inadequate adherence to medical treatment is widely acknowledged to beget high health care utilization and expenditures across a variety of chronic diseases [47]. As compliance among patients with FM is often suboptimal [5], our results are not surprising. Nevertheless, they may be conceived somehow differently. We hypothesize that the massive consumption of medications is not the result of low adherence but instead reflects a trend aimed to counteract low adherence.

We believe that our results reflect the frustration many patients and caregivers share treating the FM construct [48]. This feeling of incompetence often results in over diagnosis and overtreatment, which is discordant with accepted recommendations and guidelines treatments [49]. Moreover,

this report advocates strictly adhering to guidelines, avoiding excessive utilization of the medical infrastructure, and avoiding the prescription of medications that are inefficacious and sometimes harmful.

There are several limitations to our study. First, we did not analyze nor controlled for the cohort's co morbidities. Secondly, we did not analyze the utilization of the healthcare services and medication use according to co morbidities and whether the drugs were given prior or after the diagnosis of fibromyalgia.

In conclusion, we demonstrated the excessive utilization of health care resources amongst patients with FM in a "real life" large database. The burden is due to several factors including diagnostic difficulty, abundant comorbidities, and lack of adequate treatment.

Table 1: Characteristics of fibromyalgia subjects and controls

	Controls (71,324)	**Fibromyalgia (14,296)**	**95% CI**	**p-value**
Age	56.0±13.7	56.2±13.9	0.99-1.00	<0.001
Sex (Female)	65910 (92.4%)	13210 (92.4%)	0.93-1.07	0.978
BMI	28.0±6.01	29.1±6.20	1.03-1.03	<0.001
Socioeconomic status				
Low	27747 (39.2%)	6669 (46.8%)	0.78-0.85	<0.001
Medium	27499 (38.8%)	5397 (37.9%)	0.78-0.85	<0.001
High	15554 (22%)	2182 (15.3%)	0.55-0.61	<0.001
Smoking	19987 (28%)	4679 (32.7%)	1.20-1.30	<0.001

Abbreviations: BMI, body mass index; CI, confidence interval

Table 2: Comparative analysis of drug usage among fibromyalgia and controls

	Controls (71,324)	Fibromyalgia (14,296)	OR	95% CI	p-value
NSAID	28559 (40%)	9019 (63.1%)	2.56	2.47-2.66	<0.001
Celecoxib	1230 (1.72%)	493 (3.45%)	2.04	1.83-2.26	<0.001
Diclofenac	6538 (9.17%)	3205(22.4%)	2.86	2.73-3.00	<0.001
Etodolac	7555 (10.6%)	2646 (18.5%)	1.92	1.83-2.01	<0.001
Etoricoxib	6642 (9.31%)	2526 (17.7%)	2.09	1.99-2.20	<0.001
Ibuprofen	13496 (18.9%)	4261 (29.8%)	1.82	1.75-1.89	<0.001
Nabumetone	245 (0.34%)	82 (0.57%)	1.68	1.30-2.14	<0.001
Naproxen	2644 (3.71%)	982 (6.87%)	1.92	1.78-2.07	<0.001
Piroxicam	2325 (3.26%)	1099 (7.69%)	2.47	2.29-2.66	<0.001
Opioid	7363 (10.3%)	4683 (32.8%)	4.23	4.06-4.41	<0.001
Buprenorphine	289 (0.42%)	287 (2.01%)	4.88	4.15-5.75	<0.001
Fentanyl	188 (0.26%)	219 (1.53%)	5.89	4.84-7.16	<0.001
Morphine	45 (0.06%)	24 (0.17%)	2.67	1.60-4.35	<0.001
Oxycodone	482 (0.68%)	444 (3.11%)	4.71	4.14-5.37	<0.001
Percocet	1067 (1.50%)	737 (5.16)	3.58	3.25-3.94	<0.001
Pethidine	3 (0%)	4 (0.03%)	6.57	1.37-3.57	<0.001
Tramadol	2955 (4.14%)	1972 (13.8%)	3.7	3.49-3.93	<0.001
TCA	1467 (2.06%)	2103 (14.7%)	8.21	7.66-8.80	<0.001
Amitriptyline	1428(2%)	2070(14.5%)	8.29	7.73-8.89	<0.001
Nortriptyline	43 (0.06%)	47 (0.033%)	5.47	3.61-8.30	<0.001
Anticonvulsant	1081 (1.52%)	1266 (8.86%)	6.31	5.81-6.86	<0.001
Gabapentin	235 (0.33%)	187 (1.31%)	4.01	3.3-4.86	<0.001
Pregabalin	871 (1.22%)	1107 (7.74%)	6.79	6.20-7.43	<0.001
SSRI	6571 (9.21%)	2484 (17.4%)	2.07	1.97-2.18	<0.001
Citalopram	1798 (2.52%)	668 (4.67%)	1.9	1.73-2.07	<0.001
Fluoxetine	434 (0.61%)	178 (1.25%)	2.06	1.73-2.45	<0.001
Escitalopram	3232 (4.53%)	1182 (8.27%)	1.9	1.77-2.03	<0.001
Paroxetine	903 (1.27%)	422 (2.95%)	2.37	2.11-2.66	<0.001
Sertraline	422 (0.59%)	178 (1.25%)	2.12	1.77-2.52	<0.001
SNRI	1696 (2.38%)	2192 (15.3%)	7.43	6.96-7.94	<0.001
Duloxetine	924 (1.30%)	1547 (10.8%)	9.24	8.50-10.1	<0.001
Milnacipran	98 (0.14%)	213 (1.49%)	11	8.67-14	<0.001
Venlafaxine	719 (1.01%)	568 (3.97%)	4.06	3.63-4.54	<0.001

Abbreviations: NSAID, non-steroidal anti-inflammatory drugs; TCA, tricyclic antidepressants; SSRI, selective serotonin reuptake inhibitors; SNRI, serotonin-norepinephrine reuptake inhibitor, OR, odds ratio, CI, confidence interval

Table 3: Multivariate regression of health care services among fibromyalgia patients

Healthcare Service	OR	95% CI	p-value
Emergency Room visits	2.39	2.23 - 2.55	<0.0001
Internal medicine ward hospitalization	1.57	1.40 - 1.70	<0.0001
General Practitioner clinic visits	3.82	3.54 - 4.10	<0.0001
Rheumatology clinic visits	11.36	10.10 - 12.79	<0.0001
Pain clinic visits	36.8	33.32 - 40.71	<0.0001

Abbreviations: OR, odds ratio; CI, confidence interval

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