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Fibromyalgia: epidemiology and risk factors, a population-based case-control study in Lebanon

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Abstract

Aim: To investigate the epidemiology of fibromyalgia (FM) and assess its risk factors.

Methods: Using data from the 2009 Community Oriented Program for Control of Rheumatic Diseases (COPCORD) study conducted in Lebanon, a population-based case control study was performed. The sample included 34 FM patients, frequency matched with 136 controls free from any musculoskeletal complaints and randomly sampled from the population. The controls were frequency matched with cases by age and gender.

Results: The 34 female FM cases were prevalent cases which existed for a long period of time and all those who consulted a doctor were previously misdiagnosed. Family history of joint problems (OR = 4.93, 95% CI: 1.56–15.58) and working status (OR = 2.69, 95% CI: 1.04–6.93) were significant risk factors for FM, after adjusting for body mass index, distress level, smoking status and residence location.

Conclusion: This was the first study to address the epidemiology of FM in Lebanon and the region. The chronic nature of FM that is characterized by frequent bouts of intense disabling pain and symptoms constitutes a significant health and economic burden. Clustering of cases in coastal areas was partially explained by other factors such as body mass index, distress level, smoking and work status. The high burden of FM found in our study calls for further investigation of potential risk factors of this condition.

Key words: epidemiology, fibromyalgia.

INTRODUCTION

Fibromyalgia (FM) is becoming an increasingly common rheumatic condition.[1] According to the 2010 preliminary diagnostic criteria of the American College of Rheumatology (ACR), it is defined as having a widespread pain index (WPI) ≥ 7 and a symptom severity (SS) ≥ 5 or a WPI 3–6 and SS ≥ 9 with symptoms present at a similar level for at least 3 months and absence of any disorder that would otherwise explain the pain.[2] The prevalence of FM according to general population studies was found to be between 0.5% and 5%.[3,4] Being a syndrome that mainly affects middle-aged populations[3], it is a main cause of workplace disability and limitations in activities of daily living.[5]

The exact etiology of FM is still unclear. Age is a factor that is consistently associated with FM which is most common among the 20–50 years age group, with an increase in the risk of FM through middle age which declines thereafter.[3,6] Another well-defined risk factor is gender, with a female-to-male ratio of 7 : 1.[7] FM has

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also been linked to occupation, such as manual labor[8] and stress imposed by occupational environment.[9] Low income level has also been associated with FM.[10,11] Familial aggregation of FM is also well established in the literature.[12] Other possible risk factors of FM include obesity associated with lower pain thresholds[13,14] and low physical activity[15,16] partially explained by poor psychological status and functional abilities.[17] Smoking is associated with an increase in the severity of FM symptoms. The prevalence of depressive disorders among FM patients was found to vary between 20–80%.[18]

A recent national study done on rheumatic diseases in Lebanon[19] revealed a prevalence of 1% for FM. When compared with other countries, this prevalence is quite similar.[1,3] The 34 identified female FM cases in Lebanon were mostly in their middle ages and residing in coastal areas. This striking geographical difference in the distribution of FM deserves attention. An exploration of the profile of FM cases in Lebanon and the associated risk factors of the disease will aid in creating public health and community-oriented interventions.

MATERIALS AND METHODS

This was a case-control study derived from the national COPCORD 'Community Oriented Program for Control of Rheumatic Diseases' study conducted in Lebanon in 2009 and approved by the Institutional Review Board of the American University of Beirut.[19] Lebanon is a small Arab country situated in the Eastern Mediterranean region, with a population of around 4 million inhabitants, a total area of 10 452 m^2 and a 210 km long shoreline. Its weather is characterized by long, hot summers, and mild cool, rainy winters, with marked differences in temperature between the coastal plain, the eastern inland and the western range of mountains. The majority of the population lives in urban areas. The major cause of mortality is cardiovascular diseases. Musculoskeletal disorders are major contributors to healthy life-years lost due to disability (YLD).[20]

The national COPCORD reported a point prevalence of rheumatic diseases as 15.0%, with the most common types being soft tissue rheumatism (5.8%) and osteoarthritis (4.0%). Coastal areas had the lowest prevalence of all diseases except for FM.[19]

Multistage probability sampling was used to sample the households in an attempt to estimate the prevalence of rheumatic diseases in Lebanon and to explore their distribution by geographic location, age and gender. In order to diagnose FM, rheumatologists used the 1990 ACR classification criteria that defines FM as widespread pain for at least 3 months and the presence of at least 11 of 18 specified tender points on examination.[21] When recommended by clinicians, serological examinations and X-rays were carried out to confirm the diagnosis.

Selection of cases and controls

Cases were participants who answered affirmatively to one of the two questions on current and past pain and who met the 1990 ACR criteria for FM[21]. The questions on current and past musculoskeletal complaints were: have you had in the past 7 days any pain, tenderness, swelling or stiffness in your joints, muscles or bones? And have you ever had any pain, tenderness, swelling or stiffness in your joints, muscles or bones? Participants who answered 'yes' on any of the questions and had at least scored 4 on a visual analogue scale for pain ranging from 0 to 10 (with 0 indicating no pain and 10 indicating maximum pain), were examined after 2–5 weeks by trained rheumatologists to confirm the presence of FM according to the 1990 ACR criteria.[21] As a result, 34 female FM cases were identified and confirmed by medical examination.

Controls were participants selected from the same population of cases who reported neither current nor past musculoskeletal pain and had never received diagnosis of or treatment for rheumatic diseases. According to the 1990 ACR criteria, pain is a cardinal feature of FM.[21] Also, the sensitivity and specificity of the ACR criteria for FM are 88.5% and 81%, respectively.[21] Hence, the absence of current or past pain was sufficient to consider the controls free from FM. Controls were frequency matched with the cases by age. Four controls per case were selected (number of controls = 136) in order to enhance the power of this study in detecting any significant associations. Simple random sampling was applied to select the required number of controls in every age group.

Measures

Covariates included demographic characteristics (age, marital status), socio-economic variables (education, income, working status), geographic location (place of residence), obesity (body mass index [BMI]), behavioral risk factors (cigarette smoking, arghile smoking, alcohol drinking, physical activity), genetic predisposition (family history of joint problems) and psychological status (psychiatric distress). All variables were self-reported except for weight and height which were measured by

the field workers. The specific indicators were: marital status (married, ever married); residence location (mountain/valley and coast); level of income in Lebanese liras (LL: low income as < 750 000 LL equivalent to $US500, middle as 750 000 to 3 million LL equivalent to $ US500–2000 and high income as > 3 million LL equivalent to $US2000); level of education (low education as intermediate or below, medium as high school and high as university or technical); working status (working, nonworking); presence of any family member with any history of joint diseases; calculated BMI based on the measured weight and height in the household survey (normal BMI: < 24.9 kg/m^2, overweight: 25–29.9 kg/m^2 and obese: ≥ 30 kg/m^2); smoking status (non-smoker, current/ex-smoker); calculated mean packs per year according to the reported number of cigarettes per day; water-pipe smoking status; alcohol consumption (nondrinker, current/ex-drinker); physical activity (no physical activity, irregular and regular activity) and distress level calculated according to the General Health Questionnaire (GHQ-12 score) (no distress: 0–2, distress ≥ 3).

Statistical methods

Data analysis was performed using the softwares SPSS version 18 (SPSS Inc., Chicago, IL, USA) and STATA version 10 (StataCorp, College Station, TX, USA). Odds ratios (OR), 95% confidence intervals (CI) and *P*-values were computed through univariate and multivariable logistic regression models. A *P*-value < 0.05 was considered to be significant in the multivariable logistic regression. All variables for both groups (cases and controls) were described using frequency distributions except age and sex (the matching variables). All the covariates with a *P*-value of 0.20 or less in the univariate analysis were included in the multiple logistic regression model. Due to the small count in some variables' categories, some categories were lumped together, such as residence location (mountain with valley), monthly income (high and medium income levels), level of education (high with medium educational level), BMI (overweight and obese) and physical activity (no physical activity and irregular physical activity). Chi-squared tests and Fisher's exact tests (when the expected cell count fell below five) were used for categorical variables and independent samples *t*-test for continuous variables to test for differences between cases and controls. As for the multivariable analysis, likelihood ratio tests (LR) were used to compare full and reduced models and to determine which variables should be excluded from the models.

Table 1 Descriptive characteristics of the 34 cases of fibromyalgia

Variable	Cases *n* (%)
Pain or any problem in last week	
No	2 (5.9)
Yes	32 (94.1)
Site number involving any problem in the last week	
2–5 sites	10 (31.3)
6–9 sites	22 (68.7)
Mean of VAS score† for pain in last week (*n* = 32)	7.25 (SD 1.9)
Difficulty in doing daily activities	
No	9 (28.1)
Yes	23 (71.9)
Self-rated health on a VAS‡	
1–6	20 (71.4)
≥ 7	8 (28.6)
Having/had treatment for problems in joints, bones, muscles	
No	11 (32.4)
Yes	23 (67.6)
Treatment from doctor	
No	2 (8.7)
Yes	21 (91.3)
Other diagnoses than fibromyalgia/fibrositis	23 (100)

†VAS for pain: (0–10), 0/10 indicates no pain and 10/10 indicates most severe pain. ‡VAS for self-rated health: (0–10), 0/10 poor self-rated health and 10/10 excellent self-rated health.

RESULTS

A description of the 34 FM cases is shown in Table 1. Most of the cases were prevalent cases who existed for a long period of time; 94% of the cases reported current pain, swelling or tenderness in their joints, muscles or bones with a mean pain score on VAS (visual analogue scale) of 7.25 (SD = 1.9). The pain was chronic in 96% of the cases.

Difficulty in performing daily activites was reported by 71.9% of FM patients and reported poor self-rated health. As for the health-seeking profile, 67.6% of the cases reported having received treatment for their musculoskeletal problems from a physician. However, none of them reported being ever diagnosed with FM/fibrositis. Previous diagnoses of the cases included arthritis (11.7%), osteoarthritis (5.8%), rheumatism (14.7%), fatigue (5.8%) and ankylosing spondylitis (2.9%).

Of the study participants, 58.8% were in the 30–49 years age group (Table 2). The bivariate analysis shows that residing in coastal areas, being employed, having a family member with rheumatic diseases, being overweight/obese, being current/ex-smoker and being distressed, were all significantly associated with FM.

Table 2 Frequency distributions and bivariate associations of the study variables among cases and controls: Lebanon, 2009

Variable	Cases *n* (%)	Controls *n* (%)	Total *n* (%)	OR (95% CI)	*P*-value
Age in years					
20–29	4 (11.8)	16 (11.8)	20 (11.8)	1	–
30–49	20 (58.8)	80 (58.8)	100 (58.8)	1.00	1.00
≥ 50	10 (29.4)	40 (29.4)	50 (29.4)	1.00	1.00
Marital status					
Single	9 (26.5)	29 (21.5)	38 (22.5)	1	–
Ever married	25 (73.5)	106 (78.5)	131 (77.5)	0.7 (0.32–1.81)	0.53
Residence location					
Mountain/valley	8 (23.5)	52 (38.2)	60 (35.3)	1	–
Coast	26 (76.5)	84 (61.8)	110 (64.7)	2.01 (0.85–4.78)	0.11*
Educational level					
High (university or technical)/medium (high school)	10 (29.4)	49 (36)	59 (34.7)	1	–
Low (elementary or below)	24 (70.6)	87 (64)	111 (65.3)	1.35 (0.60–3.06)	0.47
Monthly income					
High (> *USD*2000)/*medium* (USD500–2000)	25 (73.5)	105 (80.8)	130 (79.3)	1	–
Low (< USD500)	9 (26.5)	25 (19.2)	34 (20.7)	1.51 (0.63–3.64)	0.35
Working status					
Nonworking	19 (55.9)	93 (68.4)	112 (65.9)	1	–
Working	15 (44.1)	43 (31.6)	58 (34.1)	1.71 (0.79–3.68)	0.17*
Family member with rheumatic disease					
No	18 (69.2)	111 (91)	129 (87.2)	1	–
Yes	8 (30.8)	11 (9)	19 (12.8)	4.50 (1.59–12.66)	0.006*
Body mass index (BMI)					
Normal (≤ 24.9 kg/m^2)	10 (29.4)	66 (50)	76 (42.2)	1	–
Overweight (25–29.9 kg/m^2)/obese (≥ 30 kg/m^2)	24 (70.6)	66 (50)	90 (57.8)	2.40 (1.06–5.41)	0.032*
Mean BMI (kg/m^2)	28.7 (SD 6.4)	25.3 (SD 4.0)	–	–	< 0.001*
Cigarette smoking status					
Non-smoker	16 (57.1)	88 (71.5)	104 (68.9)	1	–
Current/ex-smoker	12 (42.9)	35 (28.5)	47 (31.1)	1.88 (0.8–4.38)	0.14*
Water-pipe smoking status					
Non-smoker	24 (85.7)	97 (78.9)	121 (80.1)	1	–
Current/ex-smoker	4 (14.3)	26 (21.1)	30 (19.9)	0.62 (0.19–1.95)	0.41
Any tobacco exposure					
No	12 (42.9)	66 (53.7)	78 (51.7)	1	–
Yes	16 (57.1)	57 (46.3)	73 (48.3)	1.54 (0.67–3.53)	0.30
Alcohol consumption					
No	23 (82.1)	102 (82.9)	125 (82.8)	1	–
Yes (current/ex-drinker)	5 (17.9)	21 (17.1)	26 (17.2)	1.05 (0.36–3.09)	1.0
Physical activity					
No physical activity or irregular physical activity	24 (82.8)	106 (83.5)	130 (83.3)	1	–
Regular physical activity	5 (17.2)	21 (16.5)	26 (16.7)	1.05 (0.36–3.07)	1.0
GHQ-12 Score (distress level)					
1–2 (no distress)	21 (75)	108 (87.8)	129 (85.4)	1	–
> 3 (distress)	7 (25)	15 (12.2)	22 (14.6)	2.4 (0.87–6.60)	0.13*

*Statistically significant at $P < 0.2$. GHQ, General Health Questionnaire.

The final multivariable model presented in Table 3 include the variables that were associated with FM at the bivariate level with $P < 0.2$. Having a family member with joint disease was associated with FM (OR = 4.93, 95% CI: 1.56–15.58). Also, being employed increased the odds for FM (OR = 2.69, 95% CI: 1.04–6.93).

Table 3 Final multivariable logistic regression model: Lebanon, 2009

Variables	Adjusted OR (95% CI)	*P*-value
Residence location	2.24 (0.71–7.05)	0.17
Working status	2.69 (1.04–6.93)	0.04*
Smoking status	1.75 (0.67–4.58)	0.26
Body mass index	2.10 (0.78–5.64)	0.14
Family history	4.93 (1.56–15.58)	0.007*
Distress level	1.45 (0.44–4.82)	0.54

*Statistically significant at $P < 0.05$.

DISCUSSION

This is the first study to address the epidemiology of FM in the Lebanon region. In addition to presenting information on basic characteristics of FM patients in Lebanon, it also reveals risk factors for FM in the general population. All cases were females, mostly in the middle age category (30–50 years). This is consistent with other studies[1,3] that show age and gender as known risk factors for FM which is explained by musculoskeletal aging of the population[22] and biological, psychological and sociocultural factors responsible for the female predisposition to FM.[23–25] Most cases reported suffering severe current pain with a pain intensity similar to that reported in other studies.[11] When examined by the rheumatologists almost all the cases suffered from chronic peri-articular pain involving multiple sites. This indicates that FM is a chronic condition accompanied by frequent bouts of intense disabling pain and symptoms. The fact that FM mostly affects middle-aged individuals makes it a disorder that negatively influences the productivity and quality of life of patients both on the physical and mental levels. The majority of the cases reported difficulty in doing daily activities and when asked to assess their health status most had poor self-rated health. These findings provide further evidence on what has been previously reported by other studies on the burden of disability, whether at the workplace or in activities of daily living (ADL).[5,26] Also, studies suggest an association between chronic pain and low self-rated health[27] which is supported by our study. As for the psychological burden of FM, several studies demonstrate the distress and depressive symptoms experienced by most FM patients.[28,29]

What is most alarming is that all the cases who consulted a doctor had not been diagnosed with FM, but were given other names for their problem such as fatigue, arthritis, rheumatism, calcification, and so on. Despite the fact that more than half of the consulting physicians were rheumatologists, the FM syndrome was missed. The diagnosis of FM is definitely a challenge due to the symptoms it shares with other conditions, such as chronic fatigue syndrome and rheumatoid arthritis.[30] Therefore, continuing medical education within the field of rheumatology and training health specialists, especially rheumatologists, on the accurate diagnosis and appropriate treatment of FM are crucial to capture the disorder in its early stages, thus preventing physical de-conditioning and loss of function.

Two variables were found significantly associated with FM and these were: family history of rheumatic disease and work status.

The genetic predisposition to FM is consistent with the literature.[12,31] The possibility of pooling of certain genes associated with FM can also be a result of consanguineous marriages which has been shown to be a characteristic in Muslim Bedouin FM women.[32] Family history also points toward potential common exposures such as common living conditions, behaviors or environmental factors. This warrants further investigation in a region with a high level of consanguineous marriages.[33]

In the literature, physical and psychological stress at the workplace were found to be risk factors for the development of FM.[34] In this study, work status remained significantly associated with FM even after accounting for other factors; working females had higher odds of FM in comparison to those who did not work. Another issue in evaluating occupational factors would have been the type of job which was not measured in this study. The type of occupation has been associated with FM in several studies; risky physical workload and repetitive work has been associated with FM.[35] The small sample size prevented further categorization for type of occupation. This warrants further investigation of the occupational factors, in particular type of occupation and its relationship to the FM syndrome.

Geographical location assessed according to residence location, was associated with higher odds of FM on the coast compared to the mountains and valleys. However, in multivariate regression it lost its significance, probably due to lack of power. It was confounded by smoking status, BMI and distress. Further associations were found between smoking status and residence location where current/ex-smoking is more associated with living in coastal areas than in the mountains/valleys. Furthermore, a higher BMI was associated with being a coastal resident. These relationships suggest possible interpretations of the clustering of FM cases in the

coastal areas. In the literature, higher BMI was found to be associated with FM, where being overweight or obese compared to normal weight increased the risk for FM, risk ratios were 1.70 (95% CI: 1.35–2.13) and 1.64 (95% CI: 1.16–2.33), respectively ($P < 0.001$).[13] Also, several studies report an association between smoking and FM; chronic widespread pain (CWP) severity on a scale of 0–100 was higher for smoker FM patients (61 ± 17.6) in comparison to nonsmokers (56.1 ± 20.8) ($P = 0.05$).[36] Weingarten *et al.*'s study also showed that tobacco users had a greater FM impact questionnaire (FIQ) composite score 70 (15.1) versus nonusers 61.8 (16.8) ($P < 0.001$).[37]

Other factors might have accounted for the geographical difference in the occurrence of FM. Some potential candidates that have been described in the literature include co-morbidities such as: depression and anxiety where the risk ratios for FM in females were 2.85 (95% CI: 2.38–3.42) and 3.47 (95% CI: 3.12–3.87), respectively;[38] use of oral contraceptive/hormones where the severity of CWP on VAS was higher and the duration of CWP was longer in postmenopausal patients ($P = 0.048$ and 0.024, respectively);[39] and effect of humidity or weather conditions whereby the pain in FM was significantly correlated to low temperature and high atmospheric pressure ($r = -0.255$, $r = 0.22$, $P < 0.01$).[40] The implication is that having an indepth exploration of the etiology of the regional differences in the occurrence of FM is necessary, especially in that geographical location is an important indicator of common living conditions and exposures that are modifiable.

The case definition for FM in this study was based on the 1990 ACR criteria. If it were based on the 2010 FM diagnostic criteria we would have probably been able to identify more FM cases, as these new criteria capture the broader clinical picture and allow more appropriate diagnosis. This would have increased our sample size and hence would have provided better evidence for any associations.

Limitations

A limitation of the study is the small number of cases, which prevented the stratification of data based on some variables such as residence location, education and income. Another limitation is that the small sample size led to wide 95% confidence intervals. Also, the study included prevalent cases existing for long periods of time, which might have led to changes in the exposures secondary to the disease, such as smoking cessation or increasing physical activity after being diagnosed.

Recall bias is another limitation of this study due to self-reporting, in addition to differential recall bias, especially in the case of family history of joint problems; cases of FM are more likely to remember having any family member with similar diseases than the controls. This could have shifted the OR away from the null, creating a false association between FM and family history. Finally, the survey did not tackle other aspects which might have accounted for differences in the odds of the disease such as the use of oral contraceptive pills, co-morbidities and the use of other medications.

Strengths

This case control study was based on the data from the national cross-sectional study done on rheumatic diseases in Lebanon. The sample of this cross-sectional study was a representative sample of the Lebanese population which decreases the selection bias, a recognized limitation in most case control studies. The selection bias was also minimized by choosing controls sampled from the same population of cases. Furthermore, the effects of gender and age on FM were accounted for through the frequency matched design of this study. Moreover, some exposures such as residence location, and BMI were not subject to recall bias because they were measured by the researchers during the home visits. The cases were also clinically confirmed by trained rheumatologists. Finally, the chronic nature of the FM syndrome minimizes the possibility of any survival bias. Hence, cases do not represent those who survived the disease, but are representative of cases in the general population.

CONCLUSIONS

In Lebanon, knowledge regarding the FM syndrome is lacking. Not only is FM a disorder that is rarely recognized by the general public, but also often misdiagnosed by physicians, including specialist rheumatologists. This study provides more information on the characteristics of FM patients in Lebanon. Our results indicate a chronic nature of FM that is accompanied by bouts of severe disabling pain and symptoms and hence constituting a health and economic burden to the community. Regarding the geographical variation of FM across the Lebanese population, clustering of the cases in coastal areas was partially explained by other factors, such as BMI, distress level, smoking and work status. Our findings also add further evidence to the strong genetic background of FM.

RECOMMENDATIONS

The resulting characteristics of FM identified in this study could provide a foundation for a more focused investigation centered on selected individual factors such as stress-related factors, co-morbidities and specific occupational exposures, such as work environment and workload. Furthermore, the unequal distribution of FM in Lebanon might be an indicator of the influence of urban stress which mostly characterizes coastal areas. Identification of risk factors for FM through further research would be of great significance for prophylaxis.

Further research is needed regarding the burden of FM both on the patient and the health-care system. Finally, we recommend raising awareness about FM syndrome as a distinct life-disabling disorder, among patients and physicians who are still missing it out on a diagnosis. Training physicians on proper diagnosis and treatment are essential to decrease the burden and symptoms of FM at the individual and community levels.

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