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ORIGINAL RESEARCH

Exploring the Mediating Role of Insomnia in the Relationship Between Fibromyalgia, Depression, and Anxiety in Lebanese Adults

Abdallah Chahine[1], Christian-Joseph El Zouki[2], Ghida Al Khoury[1], Sahar Obeid[3], Feten Fekih-Romdhane[4,5], Marielle Mansour[6], Jean-Claude Lahoud[1,7], Souheil Hallit[1,8,9]

[1]School of Medicine and Medical Sciences, Holy Spirit University of Kaslik, Jounieh, Lebanon; [2]UFR de Médecine, Université de Picardie Jules Verne, Amiens, 80000, France; [3]Social and Education Sciences Department, School of Arts and Sciences, Lebanese American University, Jbeil, Lebanon; [4]The Tunisian Center of Early Intervention in Psychosis, Department of Psychiatry "ibn Omrane", Razi Hospital, Manouba, 2010, Tunisia; [5]Tunis El Manar University, Faculty of Medicine of Tunis, Tunis, Tunisia; [6]Department of Nutrition, Lebanese German University, Sahel Alma, Lebanon; [7]Department of Orthopedics, Notre Dame Des Secours University Hospital Center, Byblos, Lebanon; [8]Department of Psychology, College of Humanities, Effat University, Jeddah, 21478, Saudi Arabia; [9]Applied Science Research Center, Applied Science Private University, Amman, Jordan

Correspondence: Souheil Hallit, School of Medicine and Medical Sciences, Holy Spirit University of Kaslik, P.O. Box 446, Jounieh, Lebanon, Email souheilhallit@hotmail.com; Sahar Obeid, School of Arts and Sciences, Social and Education Sciences Department, Lebanese American University, Jbeil, Lebanon, Email saharobeid23@hotmail.com

Background: Several studies have emerged to understand the relationship between insomnia and mental health issues like depression and anxiety from a causative perspective. Lebanon is a small country tormented by war, social insecurities and economic challenges, making it the fertile ground to understand the interaction between these variables in this population, especially with chronic pain. This study aims to better understand the relationship between insomnia, depression and anxiety in fibromyalgia patients in the Lebanese context.

Methods: This cross-sectional study was conducted from October to November 2024 and involved participants from all over Lebanon. The questionnaire included sociodemographic questions and scales including the Widespread pain index (WPI), Symptom severity scale (SSS), Patient Health Questionnaire (PHQ-4) and Insomnia Severity Index (ISI).

Results: The analysis showed that Insomnia mediated the association between fibromyalgia and depression; higher fibromyalgia was significantly associated with higher insomnia severity, whereas higher insomnia severity was associated with higher depression. Also, Insomnia mediated the association between fibromyalgia and anxiety; higher fibromyalgia was significantly associated with higher insomnia severity, whereas higher insomnia severity was associated with higher anxiety. However, depression and anxiety did not mediate the association between fibromyalgia and insomnia severity.

Conclusion: This study focused on the mediating role of insomnia between fibromyalgia and development of depression and anxiety on a sample of 641 Lebanese individual. With the use of specific scales and guidelines of the American College of Rheumatology, we were able to clearly elucidate the relationship between the selected variables. These findings underscore the importance of addressing issues such as insomnia in chronic pain as well as the associated comorbidities which have been proven to play an important role in the course of the disease. Future research should further explore targeted interventions that could enhance overall wellbeing in individuals with FM, considering the multiple factors influencing one's condition.

Keywords: fibromyalgia, depression, insomnia, anxiety

Background

Fibromyalgia is a common rheumatological disorder that is characterized by widespread pain in the body.[1] The pain described as musculoskeletal of nature is often accompanied by other symptoms like sleep disturbances, mood dysregulations, chronic fatigue and cognitive difficulties.[2] This multifactorial syndrome is categorized as nociplastic pain, having the central nervous system as a main generator of pain and the main driving force behind its complex pathophysiology that is still a subject of study and debate.[3] The lack of biological markers and a tangible laboratory

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measure of Fibromyalgia leads to confusion and often false diagnosis of this interesting and challenging disorder.[4] No clear etiology has been identified, but studies showed possible involvement of multiple factors including genetic predisposition, environmental exposure, stressful and psychological precursors, inflammatory components and possibly autoimmune contribution.[5–7] Other risk factors include low socioeconomic status, obesity, smoking and low physical activity.[8–11] Some authors suggest that fibromyalgia can be triggered by physical trauma, surgery or significant stress, whereas others found that some patients do not have a single triggering event but accumulated symptoms with time.[12,13] Studies showed that patients with the disorder have a neurotransmitter imbalance in the brain, mainly due to elevation of levels of neurotransmitters that are excitatory in nature such as Glutamate and Substance P and a decrease in levels of other neurotransmitters like serotonin and norepinephrine in the spinal cord.[14–17]

Numerous studies focused on the possible relationship between fibromyalgia and other conditions like Major depressive disorder, Anxiety and Insomnia.[18] Authors concluded over the years that fibromyalgia almost always co-exists with other mental health conditions, mainly because of the negative effect of this debilitating disorder on the patient's wellbeing and physical health.[19] But, the exact relationship between these components remains a matter of debate, as they are discovered at about the same time; hence, more studies are needed to evaluate the nature of the relationship between these elements and how they exhibit their influence, by elevating or reducing each other's effect in patients with fibromyalgia.

The Relationship Between Fibromyalgia, Anxiety and Depression

Major depressive disorder is defined as a mood disorder that affects how the person feels, reacts and interacts with people and his surroundings.[20] According to the DSM-5, depression should occur for a minimum of two weeks with a depressed mood or a markedly diminished interest or pleasure and other important symptoms like insomnia or hypersomnia, fatigue, loss of energy and diminished ability to think among others.[21] Depression is a common disorder that is on an exponential rise for the past decade, especially in the younger population and mainly in females.[22,23] Depression not only affects someone's mental health, but also has a devastating effect on their physical wellbeing.[24] Patients experiencing depression complain mainly of changes in appetite or weight, feeling tired and body aches all the time.[21] Some studies suggest that depression can manifest in physical forms like gastrointestinal problems, joint pain, back pain and chronic fatigue, but the most alarming sequela of depression remains suicide.[25,26] There is strong evidence that suggests that depression and fibromyalgia are related to each other with a prevalence of depression of at least 40% in fibromyalgia patients.[27] These two disorders can coexist, have comparable pathophysiology and can be treated with similar pharmacological agents which lead to the theory that depression and fibromyalgia are a mosaic of symptoms of a single underlying condition and possibly classifying fibromyalgia as part of the family of affective disorders that include psychiatric and somatic conditions.[28,29] Generalized anxiety disorder (GAD), on the other hand, is defined as excessive anxiety and worry occurring for at least 6 months with symptoms occurring more days than not.[30] The person suffering from anxiety finds it difficult to control the worry, and experiences at least 3 of these 6 symptoms: restlessness, being easily fatigued, irritability, difficulty concentrating, muscle tension and sleep disturbance.[31] This common, woman-dominant disorder is a persistent feeling of worrying that affects all aspects of life from finances to social interactions and being on time, developing slowly with a pic between the age of 30 and 44, but can be present in childhood.[32] According to a study assessing anxiety and quality of life in fibromyalgia patients, it was assumed that fibromyalgia patients have a worse quality of life and higher levels of anxiety and high levels of tension, nervousness and preoccupation.[33,34] Aparicio et al suggest that higher reported pain, but not higher tenderness was linked to higher levels of anxiety. Also, there was a larger chance of severe fibromyalgia in patients with higher levels of anxiety.[35] Another study published in the Journal of Behavioral Medicine concluded that illness uncertainty in fibromyalgia patients is associated significantly with anxiety, avoidance and passive coping, underlying the strong relationship between anxiety and fibromyalgia.[36]

The Relationship Between Fibromyalgia and Insomnia

Sleep disturbances can be classified as insomnia or the inability to sleep or hypersomnia or oversleeping.[37] Insomnia is defined as the inability to fall asleep, stay asleep, not sleeping well or not sleeping enough.[38] Consequently, insomnia has repercussions on daytime activities, such as delayed reflexes, memory problems and concentration trouble, disruptions in

work and social routines and feeling tired or sleepy.[39] This condition can be caused by multiple of factors such as a family history of sleep conditions, difference in brain neurotransmitter balance and medical conditions such as acid reflux, Parkinson's disease and chronic conditions related to pain.[40] It is worth noting that the long effect of sleep deprivation can manifest in physical forms but also mental health issues; therefore, complications of this condition are depression, anxiety, hypertension and stroke.[41,42] Obstructive sleep apnea (OSA) is a disorder of sleep that have found to be related with fibromyalgia.[43] OSA is a sleep disorder in which a person's upper airway becomes partially or completely obstructed during sleep, leading to repeated pauses of breathing called apneas.[44] A significant overlap between sleep apnea and fibromyalgia exists as each condition may worsen the other.[45] OSA may worsen FM by disrupting restorative sleep and increasing central pain sensitivity. That is why, screening and treating OSA in fibromyalgia patients can lead to symptoms improvement.[46] Regarding insomnia and fibromyalgia, a study conducted in 2012 by Consoli et al described a lower quality of life in patients with Fibromyalgia, having difficulty falling asleep because of the severity of their pain.[47] Baker et al describes the comorbidity rate between insomnia and musculoskeletal pain between 50% and 80%.[48] Fibromyalgia patients have increased frequency of wake and sleep short period but decreased bout duration, demonstrating their inability to maintain a continuous sleep.[49] An interesting 2018 study about the changes in gray matter following cognitive behavioral therapy for insomnia (CBT-I) in patients with comorbid Fibromyalgia and Insomnia found that CBT-I may slow down or even reverse gray matter atrophy in patients with the comorbidity.[50] Although the association between pain and insomnia is bidirectional, research over the past decade suggests that sleep impairment may have a stronger impact on chronic pain than vice versa.[51]

The Interactions Between Fibromyalgia, Depression, Anxiety and Insomnia

Several studies have emerged to understand the relationship between insomnia and mental health issues like depression and anxiety from a causative perspective. In a study entitled "depression and insomnia: questions of cause and effect", authors wanted to know what condition causes the other viewing the close relationship between sleep and mood regulations. They concluded that sleep deprivation works as a catalyst for antidepressant activity as insomnia disappears when depression is treated, showing that insomnia works as a mediator of depressive illnesses and that depression can be considered a complication of insomnia.[52] In another study published in the American Journal of Hypertension, insomnia was found to be the mediator between depression and the incidence of hypertension, suggesting that treating insomnia in depressed patients can decrease the risk of development of cardiovascular diseases.[53] On the other hand, Mason et al in an attempt to study insomnia before and after the treatment of anxiety and depression concluded that compared with people without insomnia, people suffering from insomnia have more severe symptoms of anxiety and depression, highlighting the importance of insomnia in anxiety and depressive disorders.[54]

In a meta-analysis of 11 randomized controlled trials of patients with chronic pain, Tang and colleagues found that treatments incorporating at least one CBT-I component improved sleep, pain, depression and fatigue in chronic population, underlying the effect of insomnia on mental health.[55] This conclusion is supported by other studies, for example, Ye et al found that because individuals with chronic pain are susceptible to symptoms of anxiety and depression, treating insomnia has been associated with improvement in these symptoms,[56] and, Cunningham et al concluding that the improvement in depression could be mediated by the improvement in insomnia.[57] Hence, the impact of pain on anxiety and depression is mediated by objective and subjective sleep characteristics in fibromyalgia patients,[58] but more studies are needed to evaluate the impact of sleep disturbances, particularly insomnia, on improving anxiety and depression in patients with Fibromyalgia who have more severe symptoms at baseline.[59]

The Present Study

In Lebanon, a small country in the middle east, there is a scarcity of data regarding fibromyalgia, its epidemiology and correlates.[60] Recent studies suggest that the prevalence of fibromyalgia in Lebanon in the general population is estimated to be 7%, one of the highest rates in the world.[60–62] This small country is tormented by war, social insecurities and economic challenges, making it the fertile ground to understand the relationship between insomnia, depression and anxiety in this population.[63] A study suggested that about 26% of Lebanese young adults suffer from depression and 28% from anxiety disorders owing to the high prevalence of mental health issues in Lebanon.[64] Regarding insomnia, in an attempt to study the

prevalence of this disorder in the Lebanese population, Al karaki et al, suggested that about 47% of Lebanese adults suffer from insomnia, a number that is considered immense in regard to the 12% approximation of insomnia in the population.[65] This being said, a country with one of the highest rates in the world of fibromyalgia, insomnia, depression and anxiety is the perfect place to study the causative relationship between those variables. This study aims to better understand the relationship between insomnia, depression and anxiety in fibromyalgia patients in the Lebanese context. The objective of our study is to assess the role of insomnia in mediating the relationship of fibromyalgia with anxiety and depression and the role of anxiety and depression in mediating the relationship between fibromyalgia and insomnia.

We hypothesize that insomnia mediates the relationship between anxiety and depression and that anxiety and depression can possibly mediate the relationship between fibromyalgia and insomnia.

Methods

Ethics Approval

The study was carried out in accordance with the ethical guidelines laid down by the Ethics Committee of Notre Dame des Secours University Hospital. Every subject was fully informed about the purpose of the research study, the confidentiality of their data, their rights, and the voluntary basis of participation. All participants signed their informed consent. This study was conducted in accordance with the principles of the Declaration of Helsinki.

Study Design and Participants

This survey followed the cross-sectional design. It was conducted from October to November 2024, within a period of five months, enrolling Lebanese adults from all over the country. A 20-minute online survey link was forwarded through the snowball method using social media and messenger apps. We included participants above the age of 18, residents of Lebanon, and those who would consent to participate in the study. People suffering from comorbidities known to be a differential diagnosis for CWP (chronic widespread pain) and FM were excluded in this study like rheumatoid arthritis and polymyalgia rheumatica among others.

Questionnaire

This survey was carried out in the Arabic language, divided into several sections: the first section contained the purpose of the study and the electronic consent form before the start of the study. The second section outlined the general information on socio-demography, including age, sex, and financial distress (evaluated through one question rated from 1 to 10, with 10 indicating highest level of financial burden).[66] Physical activity Index was assessed by multiplying the daily activity intensity, frequency and duration.[67] The third is health-focused and covers questions on BMI, history of medical and surgical conditions, and major conditions of interest: polymyalgia rheumatica, spondylarthritis, inflammatory myopathy, systemic inflammatory arthropathies, and hypothyroidism. Smoker status was evaluated using pack years, and alcohol consumption was assessed based on questions about the number of drinks one usually consumes per week. The last section included these scales and indexes.

All patients that suffer from a disease that induces musculoskeletal pain are not excluded from the study with respect to the latest guidelines of the ACR.[68]

According to the new preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity issued in 2010 by the ACR and modified in 2016, a patient must satisfy 3 conditions. First, the patient should have the symptoms at a similar level for at least 3 months. Secondly, the patient should have a WPI greater than or equal to 7 and a SS score of 5 or more, or a WPI score between 4 and 6 and a SS score that is greater than or equal to 9.[69,70] Third, pain must be present in at least 4 of 5 specific regions defined as Left and Right upper regions, axial region, and Left and Right lower regions. The jaw, chest and abdominal pain are not included in the specific regions.[71]

Widespread Pain Index (WPI)

Validated in Arabic,[72] the Widespread Pain Index uses a list of 19 body areas where the patient felt pain over the past week. The total number of body areas is equated to the score given; therefore, the WPI score can range from 0 to 19. The

body areas that are covered by this scale include: the neck, jaw, shoulder girdle, upper and lower arm, chest, upper and lower back, abdomen, hip, upper and lower leg. Each area counts as 1, and the left side is differentiated from the right in the scoring system.[73,74]

Symptom Severity Scale (SSS)

Validated in Arabic,[72] the Symptom Severity Scale on the other hand is divided into two parts: levels of severity and other somatic symptoms. Concerning the first part, three categories of symptoms (fatigue, waking unrefreshed and cognitive symptoms) are graded using a scale from 0 to 3 for each category. A 0 on the scale signifies no problem; 1 a slight or mild problem but generally mild or intermittent; 2 a moderate considerable problem and is often present and/or at a moderate level and finally 3 representing a severe, pervasive, continuous and life-disturbing problem. Patients can choose one level of severity for each of the three categories according to the level of their symptoms over the past week. The total after the sum of the 3 categories varies from 0 to 9. The second part determines the extent of somatic symptoms affecting the patient's life.[75,76]

Patient Health Questionnaire (PHQ-4)

The PHQ-4 is a brief 4-item scale that is used to evaluate symptoms of depression and anxiety throughout the previous two weeks. Validated in Arabic,[77] it consists of two sub-scales: Depression (eg, "Little interest or pleasure in doing things") and Anxiety (eg, "Feeling nervous, anxious or on edge"). It consists of a 4-points Likert scale, with 0 denoting "not at all" and 3 denoting "almost every day". The sum of the scores for each of the four PHQ-4 items determines the final score. A score of three and above indicates mild psychological anguish, 6 to 8 indicates moderate psychological distress, and 9 to 12 indicates severe psychological distress.[78]

Insomnia Severity Index (ISI)

One of the most well-known tools for assessing insomnia is the ISI. Validated in Arabic,[79] it comprises a self-administered, widely used 7-item questionnaire that focuses on the DSM IV diagnostic criteria for insomnia, particularly created to assess how patients perceive insomnia and how it affects their quality of life, ability to operate daily and to maintain their sleep, and their level of concern about their sleeping problems.[80]

Statistical Analysis

The SPSS v.27 software was used for statistical analysis. The depression, anxiety and insomnia severity scores were normally distributed since the skewness and kurtosis values were between the −1; +1 interval. The Student's *t*-test was used to compare a continuous variable and a dichotomous variable and Pearson's test to correlate two continuous variables. Bonferroni correction was applied to account for multiple testing; the corrected p value was computed as 0.05/24 (number of variables to be tested) = 0.002. The moderation analysis was performed using PROCESS MACRO (a SPSS add-on) v3.4 Model 4, with the number of bootstrap samples set at 5000 and a 95% confidence interval. Four pathways resulted from this analysis: pathway A of the independent variable to the mediator, pathway B of the mediator to the dependent variable, pathways C and C' indicating the total and direct effects of the independent variable to the dependent variable. We considered the mediation analysis to be significant if the confidence interval did not pass by zero. Covariates entered in the model were those that showed a significant p value after Bonferroni correction in the bivariate analysis. $P < 0.05$ was considered statistically significant.

Results

Participants

In total, 641 participants participated in this study, with a mean age of 35.11 years and 70.5% females. Other descriptive statistics of the sample can be found in Table 1.

Table 1 Sociodemographic and Other Characteristics of the Sample (N=641)

Variable	N (%)
Sex	
Male	189 (29.5%)
Female	452 (70.5%)
Education level	
Primary school	11 (11.7%)
Complementary school	23 (3.6%)
Secondary school	90 (14%)
Bachelor's degree	331 (51.6%)
Master's degree	147 (22.9%)
Doctorate	39 (6.1%)
Marital status	
Married	286 (44.6%)
Widowed	12 (1.9%)
Divorced	13 (2%)
Separated	6 (0.9%)
Single	270 (42.1%)
In a relationship	54 (8.4%)
Employment	
Unemployed	81 (12.6%)
Employed	282 (44%)
Self-employed	110 (17.2%)
Student	159 (24.8%)
Retired	8 (1.2%)
Hypertension (Yes)	81 (12.6%)
Diabetes (Yes)	33 (5.1%)
Dyslipidemia (Yes)	101 (15.8%)
Hyperuricemia (Yes)	18 (2.8%)
Kidney disease (Yes)	14 (2.2%)
Cancer (Yes)	16 (2.5%)
Respiratory disease (Yes)	49 (7.6%)
Neurological disease (Yes)	28 (4.4%)
Cardiovascular disease (Yes)	14 (2.2%)

(*Continued*)

Table 1 (Continued).

Variable	N (%)
Endocrine disease (Yes)	30 (4.7%)
Gastrointestinal disease (Yes)	68 (10.6%)
Dermatological disease (Yes)	29 (4.5%)
Genitourinary disease (Yes)	14 (2.2%)
Waterpipe smoking (Yes)	175 (27.3%)
Cigarette smoking (Yes)	124 (19.3%)
Fibromyalgia (Yes)	38 (5.9%)
	Mean ± SD
Age (years)	35.11 ± 12.67
Household overcrowding index (person/room)	1.14 ± 0.97
Financial satisfaction	4.8 ± 2.50
Body mass index (BMI)	25.29 ± 7.36
Physical activity	25.8 ± 19.95

Bivariate Analysis of Factors Associated with Depression, Anxiety and Insomnia

Females had a higher mean depression score compared to males. Females vs males, having gastrointestinal disease and smoking waterpipe were significantly associated with higher mean anxiety scores. Having hypertension, diabetes, dyslipidemia, hyperuricemia, neurological diseases, gastrointestinal disease and fibromyalgia were significantly

Table 2 Bivariate Analysis of Factors Associated with Depression, Anxiety and Insomnia Severity

Variable	Depression			Anxiety			Insomnia Severity		
	Mean ± SD	p	Effect Size	Mean ± SD	p	Effect size	Mean ± SD	p	Effect Size
Sex		**<0.001**	0.306		**<0.001**	0.394		0.044	0.167
Male	1.98 ± 1.83			1.75 ± 1.94			10.52 ± 5.46		
Female	2.57 ± 1.96			2.54 ± 2.05			11.51 ± 6.14		
Education level		0.037	0.199		0.119	0.156		0.840	0.020
Secondary or less	2.09 ± 1.81			2.05 ± 1.98			11.12 ± 5.55		
University level	2.47 ± 1.96			2.37 ± 2.06			11.24 ± 6.06		
Marital status		0.442	0.061		0.387	0.070		0.031	0.175
Unmarried	2.35 ± 1.93			2.24 ± 1.96			10.75 ± 5.50		
Married	2.47 ± 1.95			2.38 ± 2.16			11.79 ± 6.45		
Employment		0.907	0.009		0.303	0.084		0.722	0.029
Unemployed	2.41 ± 1.96			2.41 ± 2.02			11.12 ± 5.76		
Employed	2.39 ± 1.93			2.24 ± 2.07			11.29± 6.09		

(*Continued*)

Table 2 (Continued).

Variable	Depression			Anxiety			Insomnia Severity		
	Mean ± SD	p	Effect Size	Mean ± SD	p	Effect size	Mean ± SD	p	Effect Size
Hypertension		0.165	0.165		0.144	0.202		**<0.001**	0.456
No	2.36 ± 1.91			2.25 ± 1.99			10.88 ± 5.81		
Yes	2.68 ± 2.11			2.67 ± 2.41			13.57 ± 6.45		
Diabetes		0.160	0.311		0.038	0.453		**<0.001**	0.923
No	2.37 ± 1.91			2.26 ± 2.02			10.94 ± 5.50		
Yes	2.97 ± 2.37			3.18 ± 2.42			16.33 ± 6.71		
Dyslipidemia		0.320	0.113		0.471	0.087		**<0.001**	0.404
No	2.36 ± 1.92			2.28 ± 2.0			10.84 ± 5.77		
Yes	2.58 ± 2.05			2.46 ± 2.31			13.23 ± 6.57		
Hyperuricemia		0.360	0.289		0.295	0.349		**<0.001**	0.991
No	2.38 ± 1.92			2.29 ± 2.02			11.05 ± 5.87		
Yes	2.94 ± 2.51			3.00 ± 2.79			16.89 ± 6.42		
Kidney disease		0.955	0.015		0.376	0.240		0.023	0.614
No	2.40 ± 1.94			2.30 ± 2.04			11.14 ± 5.95		
Yes	2.43 ± 2.17			2.79 ± 2.29			14.79 ± 5.74		
Cancer		0.220	0.311		0.612	0.128		0.596	0.134
No	2.41 ± 1.93			2.30 ± 2.04			11.20 ± 5.95		
Yes	1.81 ± 1.97			2.56 ± 2.28			12.0 ± 6.45		
Respiratory disease		0.903	0.018		0.383	0.130		0.084	0.257
No	2.40 ± 1.93			2.29 ± 2.04			11.10 ± 5.98		
Yes	2.37 ± 1.91			2.55 ± 2.14			12.63 ± 5.64		
Neurological disease		0.704	0.073		0.346	0.190		**0.001**	0.541
No	2.39 ± 1.95			2.29 ± 2.05			11.08 ± 5.98		
Yes	2.54 ± 1.75			2.68 ± 2.11			14.29 ± 4.70		
Cardiovascular disease		0.825	0.060		0.376	0.240		0.175	0.367
No	2.40 ± 1.94			2.30 ± 2.04			11.17 ± 5.97		
Yes	2.29 ± 1.90			2.79 ± 2.55			13.36 ± 5.47		
Endocrine disease		0.209	0.235		0.323	0.185		0.673	0.079
No	2.38 ± 1.93			2.29 ± 2.04			11.20 ± 5.96		
Yes	2.83 ± 2.05			2.67 ± 2.26			11.67 ± 5.99		
Gastrointestinal disease		0.007	0.391		**<0.001**	0.522		**<0.001**	0.557
No	2.32 ± 1.90			2.19 ± 1.99			10.87 ± 5.82		
Yes	3.07 ± 2.13			3.25 ± 2.30			14.15 ± 6.38		

(*Continued*)

Table 2 (Continued).

Variable	Depression			Anxiety			Insomnia Severity		
	Mean ± SD	p	Effect Size	Mean ± SD	p	Effect size	Mean ± SD	p	Effect Size
Dermatological disease		0.263	0.213		0.134	0.285		0.384	0.166
No	2.38 ± 1.94			2.28 ± 2.05			11.26 ± 5.97		
Yes	2.79 ± 1.93			2.86 ± 1.98			10.28 ± 5.90		
Genitourinary disease		0.635	0.128		0.924	0.026		0.366	0.244
No	2.39 ± 1.94			2.30 ± 2.05			11.19 ± 5.97		
Yes	2.64 ± 1.78			2.36 ± 2.10			12.64 ± 5.44		
Waterpipe smoking		0.010	0.228		**0.001**	0.296		0.028	0.195
No	2.28 ± 1.90			2.14 ± 2.0			10.90 ± 5.92		
Yes	2.72 ± 2.02			2.74 ± 2.12			12.06 ± 6.01		
Cigarette smoking		0.172	0.137		0.129	0.152		0.186	0.132
No	2.35 ± 1.93			2.25 ± 2.02			11.07 ± 6.08		
Yes	2.61 ± 1.97			2.56 ± 2.17			11.85 ± 5.39		
Fibromyalgia		0.013	0.418		0.005	0.472		**0.002**	0.523
No	2.35 ± 1.93			2.25 ± 2.03			11.03 ± 5.98		
Yes	3.16 ± 1.95			3.21 ± 2.08			14.13 ± 4.89		

Notes: Numbers in bold indicate significant p value after Bonferroni correction (p ≤ 0.002).

Table 3 Pearson Correlation Matrix

	1	2	3	4	5	6
1. Depression	1					
2. Anxiety	**0.78*** **	1				
3. Insomnia Severity	**0.50*** **	**0.51*** **	1			
4. Age	− 0.08*	− **0.11****	− 0.04	1		
5. Body Mass Index	0.01	− 0.02	0.04	**0.19*** **	1	
6. Household overcrowding index	0.06	**0.13*** **	0.08*	0.02	−0.02	1
7. Financial satisfaction	− **0.21*** **	− **0.19*** **	−**0.20*** **	−0.05	0.01	− 0.05
8. Physical activity	− **0.19*** **	− **0.16*** **	−**0.17*** **	− 0.02	0.06	− 0.4

Notes: *p <0.05; **p <0.01; ***p < 0.001. Numbers in bold indicate significant p value after Bonferroni correction (p ≤ 0.002).

associated with higher insomnia severity (Table 2). Moreover, higher physical activity and financial satisfaction were significantly associated with lower depression, anxiety and insomnia severity, whereas higher household crowding index was significantly associated with higher anxiety (Table 3).

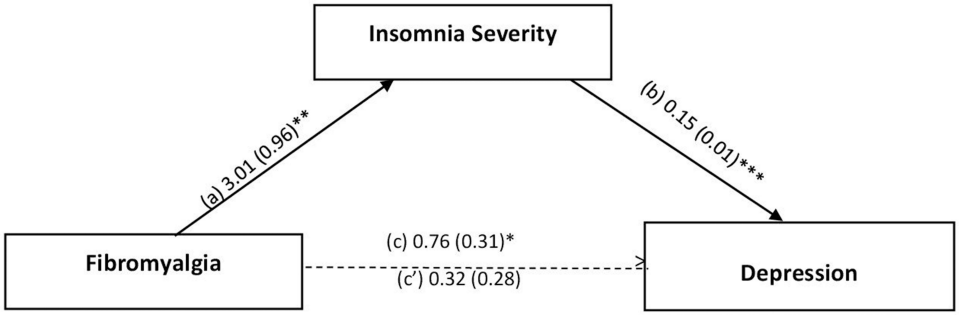

Figure 1 (a) Relation between fibromyalgia and insomnia severity (R^2= 0.083); (b) Relation between insomnia severity and depression (R^2= 0.278); (c) Total effect of fibromyalgia on depression; (c′) Direct effect of fibromyalgia on depression (R^2= 0.094). The numbers represent regression coefficients and their standard errors. *p <0.05; **p <0.01; ***p < 0.001.

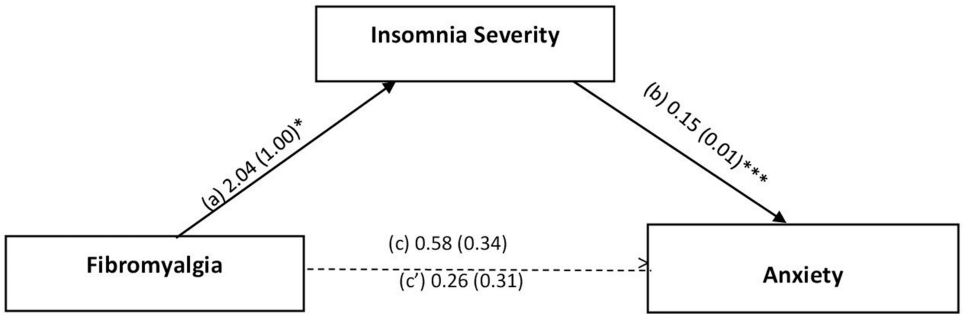

Figure 2 (a) Relation between fibromyalgia and insomnia severity index (R^2= 0.105); (b) Relation between insomnia severity index and anxiety (R^2= 0.303); (c) Total effect of fibromyalgia on anxiety; (c′) Direct effect of fibromyalgia on anxiety (R^2= 0.122). The numbers represent regression coefficients and their standard errors. *p <0.05; ***p < 0.001.

Analysis of Mediation

The mediation analysis taking depression as the dependent variable was adjusted over the following covariates: financial pressure, physical activity, and sex. Insomnia severity index (indirect effect: Beta = 0.44; Boot SE = 0.13; Boot CI 0.19; 0.70) mediated the association between fibromyalgia and depression; higher fibromyalgia was significantly associated with higher insomnia severity, whereas higher insomnia severity was associated with higher depression (Figure 1).

The mediation analysis taking anxiety as the dependent variable was adjusted over the following covariates: financial satisfaction, physical activity, sex, gastrointestinal disease, waterpipe smoking and Household overcrowding index. Insomnia severity index (indirect effect: Beta = 0.31; Boot SE = 0.14; Boot CI 0.03; 0.59) mediated the association between fibromyalgia and anxiety; higher fibromyalgia was significantly associated with higher insomnia severity, whereas higher insomnia severity was associated with higher anxiety (Figure 2).

The mediation analysis taking insomnia severity index as the dependent variable was adjusted for the following covariates: financial pressure, physical activity, gastrointestinal disease, hypertension, diabetes, dyslipidemia, hyperuricemia and neurological disease. Depression (indirect effect: Beta = 0.846; Boot SE = 0.512; Boot CI −0.172; 1.842) and anxiety (indirect effect: Beta = 0.818; Boot SE = 0.509; Boot CI −0.192; 1.838) did not mediate the association between fibromyalgia and insomnia severity.

Discussion

The current study aimed to assess the relationship between fibromyalgia and anxio-depressive symptoms in a sample of Lebanese individuals, along with the mediating effect of insomnia. An alternative model with insomnia as dependent variable and anxio-depressive symptoms as mediators was also tested. The initial results obtained suggest that insomnia

significantly mediates the relationship between fibromyalgia and depression. Extensive analysis of the main variables helped us obtain a more meticulous understanding of their interdependence.

A study conducted a few years ago revealed through thorough analysis that fibromyalgia can in fact be considered a possible agent of insomnia development, also having a predictive value regarding the persistence of this illness.[2] More precisely, it has been incriminated as a "non-restorative sleep (NRS) syndrome" where specific sleep patterns found in FM patients, strongly correlate with symptoms such as insomnia and pain. Furthermore, an experimental study on fibromyalgia and sleep that took place in Europe conducted multiple polysomnography studies (PSG) on FM patients to better assess sleep behaviors in this targeted population.[81] Their findings revealed that they altered sleep stability through subjective physiological markers. It showed that FM patients take longer to fall asleep, and this translated to 80% to 90% having increased EEG alpha activity during non-REM sleep which reflects poor quality sleep and excessive arousal. In addition, the division of clinical immunology and rheumatology at the university of Alabama worked on FM and co-occurring conditions aiming to improve the understanding of the pathophysiology of this disease.[82] They were able to explain that the sleep disturbances can be linked to reduced energy and fatigue which enhances pain, creating a self-perpetuating cycle of worsening symptoms. This owes to the fact that decreased sleep time and NRS patterns reduce GH and IGF-1 production, which are necessary for muscle repair and healing. Subsequently, it will lead to prolong transmission of sensory stimuli from damaged muscle tissue to the CNS, heightening the pain felt. To delve further, the American college of rheumatology also published an article concerning heart rate variability analysis in FM patients which revealed exaggerated sympathetic activity during nighttime relating to the fight or flight body response, along with excessive sinus node stimulation.[83] Such information may also help in explaining the sleep disturbances associated with FM. It sheds light on intricate interaction between sleep disorders and chronic pain, highlighting a potential cause-effect relationship between FM and insomnia.

Additionally, it is important to note that the lack of restful sleep and insomnia have been known to have an impact on one's mental health. This was proven in a meta-analytic evaluation where individuals with insomnia have been found to have a twofold risk to develop depression compared to someone with no sleeping difficulties.[84] This comes in agreement with our study, where insomnia was found to increase the risk of depression and anxiety.

As a matter of fact, a study published in the journal of dialogues in clinical neuroscience revealed that individuals with sleep problems had 7.6 times more chance of developing new onset major depressive episode in the upcoming year compared to individuals with no sleep problems. This evaluation also helped determine that insomnia and other sleep disorders had the strongest predictive value of who would eventually develop major depressive disorder.[85] Also, this idea aligned with an article published by the sleep research society proving that insomnia confers a risk for the development of depression and anxiety disorders, being considered a trait of vulnerability.[86]

Furthermore, the American journal of psychiatry issued an article stating that insomnia, among other anxiety symptoms should be watched out for as a precursor of suicide and an indication of suicidal risk.[87] Such information carries a significant responsibility, necessitating careful consideration. Most importantly, for better prevention, understating the pathophysiology that lies underneath is crucial. Thus, the potential mechanism relating sleep disturbance to mental health issues were elaborated by the journal of cellular and molecular medicine proving three major hypotheses.[88] To begin with, sleep loss may increase numerous inflammatory markers by activating pathways such as factor kappa-B for instance. Inflammation itself is strongly linked to depression and higher inflammatory markers have been found in depressed people. In other words, insomnia may be a trigger of inflammation, contributing to depression. However, more research concerning this relationship has yet to be done to fully comprehend this mechanism. Also, disturbed monoamines functioning has also been implicated in this complex insomnia-anxiety-depression relationship. This emanates from the disruption of the REM sleep which alters serotonin, norepinephrine, dopamine and other monoamines secretions, and they are necessary for mood regulation as well as sleep pattern adjustment in turn. This is another hypothesis that supported the mechanism through which depression was a consequence of insomnia, and it came in agreement with a study published in the journal of clinical psychology review.[89] Both articles mentioned a third idea as well, concerning the involvement of genetic factors in the development of insomnia, depression and anxiety owing to a complete genetic overlap.[88] In greater details, it has been proven through previous studies that insomnia overlaps with major depressive disorder with numbers reaching up to 56% in females, 74% in male, and 100% with generalized anxiety

disorder.[90] This being said, understanding more specifically the involvement of genes in regulating insomnia and depression and how they interact is of great importance given the clinical relevance it may have.

Bearing in mind all that was previously stated, it is plausible to consider that fibromyalgia itself is a possible trigger of depression and anxiety. As a matter of fact, among FM patients, anxiety and depressive disorders were found to be the most frequent psychiatric associated comorbidities,[91] ranging from 13% to 63.8% and 20% to 80%, respectively. These psychiatric disorders, among others (panic attacks, OCD, dysthymia etc.) have been shown to have a much higher prevalence in patients experiencing chronic pain compared to the general population, which is an observation that aligns with the findings of our study where we were able to highlight the important role that FM plays in the development of mental health conditions. Moreover, studies even suggested that chronic pain is a risk factor for suicidal behavior, with an estimated prevalence of 16.7% in FM patients. It has been elaborated that the risk is increased in FMS due to a constellation of factors that are already usually related to increased suicidality and overlap with FM, such as being a female, poor sleep hygiene, physical comorbidities such as headache and gastric diseases.[92] This is also explained by the fact that most suicidal behaviors occur in patients with underlying psychiatric diseases, whether it is depression, mood disorders, anxiety, psychosis or other, and FM patients, as we already discussed, are vulnerable to developing the previously mentioned illnesses.[93]

The previous finding clearly reveals how fibromyalgia is linked to depression, with insomnia serving as a partial mediator in this relationship. In a more exact manner, fibromyalgia contributes to depression and anxiety as we have elaborated on, independently of insomnia, but its presence can amplify this effect. An article published in 2024 in the journal of brain and behavior through a Mendelian method aimed to investigate the relationship between chronic pain and depression, while exploring the mediating role of sleep disturbances.[94] It showed how insomnia significantly mediates this association when it is present. According to Catalá et al (2024), insomnia was found to have an indirect effect on the impact of fibromyalgia on depression and anxiety; the greater the insomnia, the more anxiety was found in patients, which in turn worsened fibromyalgia forming a vicious cycle.[18] Most importantly, insomnia's role is not indispensable for the development of mental health issues in FMS but can intensify the outcome.

On the other hand, our findings revealed that depression and anxiety did not mediate the relationship between fibromyalgia and insomnia severity. These findings are not surprising since multiple studies have shown that depression and anxiety do not cause insomnia, but the other way around. According to a study entitled sleep, insomnia and mental health, the authors concluded that insomnia may in fact be a risk factor, a transdiagnostic symptom and a comorbid condition for anxiety and depression.[95] This is explained by the role played by insomnia as a modifier of brain neuroplasticity involved in the biological mechanisms of mood disorders.[95] In contrast, a Mendelian randomization study conducted in 2022 about the causal links between major depressive disorder and insomnia determined that there is a significant correlation between MDD and insomnia and identified a gene, the TCF4 as a common gene for the mutual effects of both disorders.[96] This opens to the possibility that on the biological level, depression can be the causal agent behind insomnia and vice versa as opposed to what is generally thought of a unidirectional relation, but on the clinical level, insomnia seems to almost always take the lead. Hence, our results are in agreement with the latest knowledge about depression, anxiety and insomnia and more studies are needed to assess the causality of depression in the development of insomnia.

Based on what we have extensively discussed, it became clear that the interplay between fibromyalgia is complex and requires a solid understanding. Fibromyalgia itself was found to contribute to the development of insomnia, which implicates disturbed sleep patterns and restlessness. Those previous symptoms were found to serve as precursors for further psychological illnesses including depression and anxiety. In parallel, fibromyalgia along with its panoply of symptoms increase the risk of developing mood disorders, which can be mediated by untreated insomnia. Thus, it is crucial to recognize that depression and anxiety are not mediators in the relationship between fibromyalgia and insomnia. Instead, we were able to demonstrate a cascading effect where fibromyalgia can induce insomnia, subsequently leading to mental health issues.

Clinical Implications

Throughout the study of the mediation of insomnia on fibromyalgia and its role in developing depression and anxiety, we have been able to understand the true importance of such matter and its profound clinical implications, especially in a country like Lebanon, where political and socio-economic stressors aggravate health issues. Moreover, as we saw, fibromyalgia and mental health share a common pathway of neuroinflammatory mechanisms in response to stress. The interplay between physical pain and psychological distress creates a loop where pain will increase the body's stress response, which will then worsen inflammation and impact nociception. This will also have heavy consequences since it may entrench disability and favor the development of a negative thought pattern. Henceforth, understanding this complicated relationship between FM, depression and anxiety can potentially help clinicians in developing strategies that target physical and physiological aspects, combining different methods. In fact, economic instability and political unrest are constant factors that amplifies stress levels among the Lebanese individuals which is, as we have already highlighted, a significant contributor to both FM and insomnia; this brings us back to the role of insomnia in exacerbating the burden of FM which is already overwhelming enough. Addressing such issues while bearing in mind different factors that may exacerbate the array of symptoms associated with FMS is highly important to maximize the outcome when treating patients and preventing relapses, while also aiming towards a swift and efficient improvement.

Insomnia, as we already mentioned above, should be looked out for by clinicians, and be considered a warning sign. It can help in identifying crucial phases for intervention when treating FM patients to reduce suicide rates in such a vulnerable, in addition to the challenging background they already have. It is also important to keep in mind that FM itself is associated with depression and anxiety. These comorbid mental health conditions are already considered independent risk factors for suicide, worsened by the cultural stigma surrounding mental issues. Hence, managing FM should be done cautiously, emphasizing the need to address the interconnected conditions, which requires a multidisciplinary approach spanning from pharmacological treatment, CBT to lifestyle modifications with tailored plans.

Targeted research on the burden of FM can help fill the gap in providing valuable recommendations and tools to address this matter effectively. Starting with raising awareness to reduce stigma and encourage help seeking will go a long way. Also, practically, routine screening for depression and anxiety for instance in FM patients can help in procuring a solid base for mental health, alongside providing proper training to recognize and manage FM and its commodities, physical and psychological simultaneously. By keeping in mind, the essential constitutional elements of this disease, the healthcare system can improve treatment outcomes in the target population.

Limitations

There are several limitations that should be identified in our study. First, the study relies on self-reported data concerning insomnia, depression, and comorbid diseases, which leads to recall bias as some patients may not accurately remember events, they may under or over report certain conditions given the sensitivity of our topic as well. Thus, inaccuracy is inevitable. In addition, we relied on participants' self-reporting of diseases, without medical proof or objective measures which introduce the risk of misdiagnosis or missing data. Also, the scales used in our study are yet to be validated, which may not consistently measure the intended concepts thus leading to significant variability.

Moreover, while our study consisted of a sample of 641 Lebanese individuals, our findings may not be generalizable to populations outside the region, especially given the culture and socio-economic characteristics of Lebanese citizens. This adds to the fact that there is a sampling bias due to it not being well represented by the whole population, which alters the external validity of the study. In addition, our results included 70.5% of women compared to 29.5% of males, which means we should keep in mind the potential effect female gender has on different variables.

Conclusion

This study focused on the mediating role of insomnia between fibromyalgia and development of depression and anxiety in a sample of 641 Lebanese individual. With the use of specific scales and guidelines of the American college of rheumatology, we were able to understand the relationship between the selected variables. Our findings suggested higher fibromyalgia was associated with higher insomnia severity, and higher insomnia, in turn, was associated with higher depression and anxiety. We also found that depression and anxiety did not mediate the association between fibromyalgia and insomnia. These findings

underscore the importance of addressing insomnia in chronic pain disease as well as the associated comorbidities which have been proven to play an important role in the course of the disease. In other words, this research helps emphasize the need for comprehensive multidisciplinary support for individuals suffering from FM. Future research should further explore targeted interventions that could enhance overall wellbeing in individuals with FM, considering the multiple factors influencing one's condition.

Abbreviations

WPI, Widespread pain index; SSS, Symptom severity scale; PHQ-4, Patient Health Questionnaire; ISI, Insomnia Severity Index; ACR, American College of Rheumatology.

Data Sharing Statement

The datasets produced and/or analyzed during this study are not publicly accessible but can be obtained from the corresponding author upon reasonable request.

Ethics Approval and Consent to Participate

This study adhered to the ethical guidelines established by the Ethics Committee of Notre Dame des Secours University Hospital. Participants were thoroughly informed about the study's purpose, the confidentiality of their data, their rights, and the voluntary nature of their involvement. Informed consent was obtained from all participants.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval for the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

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