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RESEARCH ARTICLE

Headache, Migraines, Obesity and Medication Burden on Fibromyalgia Impact and Quality of Life

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ABSTRACT:
Fibromyalgia (FM) is a common, complex, and chronic pain disorder characterized by widespread musculoskeletal pain, fatigue, and tenderness in localized areas. A multitude of other central sensitization related symptoms contribute to a profound medication burden and diminished quality of life for affected individuals. We evaluated the impacts of gender, chronicity of headache, migraine, obesity and medication burden on overall FM impact. We used the following validated questionnaires: Fibromyalgia Impact Questionnaire (FIQR), Beck Depression Inventory (BDI), Central Sensitization Inventory (CSI) and measured weight and body mass index (BMI) on a large university cohort of FM subjects. We found that female subjects with FM showed a significant increase in FIQR compared to males with FM. Additionally, we noted positive correlations between weight (Wt) and FIQR, BDI and CSI; BMI and FIQR, and BMI and CSI. Fibromyalgia subjects with a history of migraines (FM-migraine) showed statistically significant increases in FIQR, BDI and CSI compared to FM subjects with no reported history of migraines (FM-non-migraine). There was a steady increase in FIQR, BDI and CSI values with an increase in the frequency of headaches in both the FM -migraine and FM -non-migraine groups. When evaluating BMI, when comparing survey responses of overweight and obese patients to normal weight patients, all FIQR, BDI and CSI values were significantly increased in the various classes of overweight except CSI for the overweight category which appeared to approach significance ($p=0.057$). There were no statistically significant differences in questionnaire responses for individuals with FM on medications relative to those on no medications. Taken together, a history of migraines and headaches, frequency of headaches and obesity may impact survey responses significantly, negatively impact quality of life and correlate with higher levels of depression but medication burden did not.

Keywords: Fibromyalgia, central sensitization, migraine, headache, obesity; medication burden

Introduction

Fibromyalgia (FM) is a common, chronic pain disorder characterized by wide-spread musculoskeletal pain, fatigue, and tenderness in localized areas[1]. This disease is often accompanied by numerous other symptoms such as sleep disturbances, cognitive issues (often referred to as "fibro fog"), and mood disorders. The multitude of systemic complaints that occur in affected individuals are broadly referred to as central sensitization related symptoms [2-9]. Individuals of all ages and ethnic backgrounds may be affected with a distinct female predominance of at least 5:1 and global prevalence rates anywhere from 2 to 5 % of the population [10]. Over the course of the last several decades, we have gained insight into possible mechanisms underlying FM all of which may in part contribute towards the clinical phenotype that characterizes this condition. The most prominent of these theories underlying pathogenesis includes central sensitization although hypotheses on salience pathways [11], bioenergetic pathways [12], and neurogenic inflammation [13] are also speculated as contributors to FM clinical presentation.

Central sensitization refers to an amplification of neural signaling within the central nervous system. Heightened sensitivity can lead to an exaggerated response to stimuli, both painful and non-painful. In addition to increased sensitization to touch, individuals may also display enhanced sensitivity to sound, smell, lights, and temperature amongst others [2,3]. Clinical manifestations might consist of widespread pain that is characteristically fluctuating in nature. Alterations in neurotransmitters like glutamate and substance P accompany this process and contribute to the amplification of pain signals and the persistence of pain in FM. Bioenergetic pathways refer to the processes within cells that involve the production and utilization of energy, such as cellular respiration and the production of adenosine triphosphate (ATP). While disturbances in cellular energy metabolism could potentially play a role in certain health conditions, there is not a well-established link between bioenergetic pathways and FM. The concept of salience and its potential role in FM is an area of interest particularly in the context of the brain's processing of pain and sensory information. Salience networks are involved in detecting and integrating relevant stimuli, which includes those related to pain and emotional experiences. They help prioritize and direct attention to important sensory and emotional information and may play a crucial role in determining the significance of pain signals during processing which would also help in deciding whether incoming sensory information is worthy of attention and response [11]. Therefore, aberrant salience processing could contribute to heightened perceptions of pain and the increased sensitivity to sensory stimuli observed in FM. Finally, neurogenic inflammation refers to the process in which nerve endings release inflammatory mediators, leading to local inflammation. This may play a role in individuals with FM, particularly those concurrently affected by small fiber neuropathy [14-18]. While this process is well-established in various pain conditions, its specific role in FM is still a subject of investigation.

Multiple studies have shown a general similarity in the sensitization processes between FM and migraine. Typical clinical features that help demonstrate sensitization in FM include evidence of allodynia and hyperalgesia following stimulation [19-20]. Similar occurrences such as tenderness of scalp and pericranial muscles during a migraine attack as well as reduction of cutaneous pain thresholds to stimuli in migraine appear to support sensitization as a component of migraine [21-22]. Reports have examined the possibility of aberrant glutamate processing in the pathophysiology of migraine; a role which has been putatively also been speculated in FM [23].

Previous studies have also displayed that chronicity of migraines appears to be more impactful on FM quality of life rather than episodic migraine. Co-occurrence of comorbid conditions such as chronic fatigue syndrome occur more in chronically rather than episodically affected subjects. Finally, prevention of headache chronification in migraine patients appeared to be important in preventing the frequency of flareups of FM [24-29].

Our group has had a long-term interest in investigating the factors that exacerbate or worsen FM symptoms as measured by validated self-report scales [30-35]. As part of our studies evaluating initiating and aggravating factors for FM, we evaluated survey responses of FM subjects to determine what characteristics might be most impactful in contributing to negative effects on FM subject's quality of life. We focused on specific survey elements within the Central Sensitization Inventory (CSI)[36] and assessed their impact on the Fibromyalgia Impact Questionnaire (FIQR) [37]. The primary objectives of our study were to evaluate the frequency of self-reported migraine and headache in our study population and determine if frequency of headache correlated with worsening of FIQR and CSI. Furthermore, we wanted to assess the role of obesity and medication burden on our study population. Analysis of these key demographic profiles and questionnaire responses from a large cohort of well characterized FM subjects

evaluated in a university referral center for patients with FM and related disorders (Fibromyalgia / Central Sensitization Clinic) may provide future insight towards identifying specific subsets of FM that might be fruitful targets for personalized therapeutic interventions.

Methods

2.1 PATIENT RECRUITMENT

Approval from the University of Texas at Austin institutional review board was obtained prior to embarking on any human subjects' studies. All studies adhered to Declaration of Helsinki principles. IRB approval date was (study no. 2020030008) 19 June 2020. Criteria for the diagnosis of FM included: age 18–80 with a history of FM and meeting current criteria for FM [38-40]. Following informed consent, all subjects were examined by clinical staff. Weight (Wt) in kilograms was obtained as well as height in centimeters and BMI. Subjects provided self-report of symptoms through use of the Revised Fibromyalgia Impact Questionnaire (FIQR), a 10-item self-rating instrument that measures physical functioning, work status, depression, anxiety, sleep, pain, stiffness, fatigue, and wellbeing [37]. The Beck Depression Inventory (BDI) is a 21-item, self-report rating inventory that measures characteristic attitudes and symptoms of depression [41-42]. The Central Sensitization Inventory (CSI) is a two-part patient-reported outcome measure that assesses somatic and emotional symptoms common to CSS [36].

2.2 STATISTICAL ANALYSIS

Sigmaplot v15.0 and SigmaStat v4.0 software (Inpixon, Palo Alto, CA, USA) were utilized for statistical analysis of questionnaires and plot generation. Descriptive statistics are presented as mean ± standard deviation (SD), range, or total number of subjects (n). Pearson correlation coefficients were used to estimate the correlation between the survey measures or vital statistical indices. P-values were used to test the null hypothesis of the correlation amongst the level of questionnaire responses. Student t test was used to compare groups as appropriate. All calculated p-values were two tailed. $P < 0.05$ was considered statistically significant.

Results

3.1. CLINICAL CHARACTERISTICS OF SUBJECTS

The University of Texas at Austin as part of its University of Texas Health Austin (UTHA) multispecialty clinics has a Fibromyalgia/ Central Sensitization Clinic which has been in existence since September 2020. The clinic focuses on comprehensive care of individuals with FM and related syndromes. Typical patient diagnoses evaluated and followed in the clinic since its inception include FM, Chronic Fatigue Syndrome/Myalgic Encephalomyelitis, Myofascial Pain Syndrome, Ehlers Danlos Syndrome, Benign Hypermobility Syndromes and patients with Long Covid. For the purposes of these analyses, encounters were recorded with subjects who met ACR criteria for FM at the UTHA clinics. The clinical characteristics of the patients with FM, are presented in Table 1. There were 46 male and 590 female subjects who completed questionnaires.

Male subjects with FM (n=46) had a mean age of 41.0±13.6 with a range of 18-69. Their mean weight was 95.9± 27.1 with a mean BMI of 29.1± 7.4. Mean FIQR was 41.4±18.1. The mean CSI was 59.2± 15.4 with BDI of 21.5±10.1. Female subjects with FM (n =590) had a mean age of 43.1±13.8 with a range of 18 - 75. Their weight was 85.9± 26.2, BMI was 31.9± 9.2, with a mean FIQR of 54.2±19.6. The CSI was 61.7±15.3 with a BDI of 20.1±10.8. There were statistically significant differences between male and female values as noted in Table 1 for weight, BMI, and FIQR ($p<0.05$).

Table 1. Clinical characteristics of all subjects. Male (M) and Female (F). Values expressed as Mean +/- sd; N=number of subjects, Age (range). Weight, BMI: body mass index, FIQR: Fibromyalgia impact questionnaire revised, BDI: Beck depression index, CSI: Central Sensitization Inventory. *Statistical significance by t test <0.05.

	M	F	P
N	46	590	
Age	41.0±13.6	43.1±13.8	0.257
Range	18-69	18-75	
Weight	95.9±27.1	85.9±26.2	0.008*
BMI	29.1±7.4	31.9±9.2	<0.001*
FIQR	41.4±18.1	54.2±19.6	<0.001*
BDI	21.5±10.1	20.1±10.8	0.317
CSI	59.2±15.4	61.7±15.3	0.379

Table 2. Pooled clinical characteristics of all subjects. (male and female subjects from Table 1). Values expressed as Mean +/- sd; N=number of subjects, Age (range). Weight, BMI: body mass index, FIQR: Fibromyalgia impact questionnaire revised, BDI: Beck depression index, CSI: Central Sensitization Inventory.

	All FM
N	636
Age	43.5±14.0
Range	18 - 75
Weight	86.8±26.3
BMI	31.8±9.1
FIQR	53.4±19.9
BDI	20.2±10.8
CSI	61.6±15.0

Table 2 reflects the pooled data for all subjects with FM (both male and female subjects) evaluated in the study. All subjects with FM (n=636) had a mean age of 43.5±14.0 with a range of 18-75. Their weight was 86.8±26.3 with a BMI was 31.8±9.1, FIQR of 53.4±19.9, CSI was 61.6±15.0, MPI of 94.4±47.3, BDI of 20.2±10.8. and a VAS of 5.8±2.2.

3.2. PEARSON CORRELATIONS OF SURVEYS

Table 3 displays the Pearson correlation coefficients and P values for the survey instruments. The pairs of variables with positive correlation coefficients and P values below 0.050 tend to increase together. If a pair were to have a negative correlation coefficients and P values below 0.050, then one would anticipate that one variable would tend to decrease while the other increases. That is not seen with the current set of pair wise comparisons. For pairs with p values greater than 0.050, there is no significant relationship between the two variables.

Table 3. Pearson correlation values of survey elements of all subjects. Weight, BMI: body mass index, FIQR: Fibromyalgia impact questionnaire revised, BDI: Beck depression index, CSI: Central Sensitization Inventory. Significance by one-way ANOVA. Correlation Score / p value.

Score	**Wt**	**BMI**	**FIQR**	**BDI**	**CSI**
Wt	1.00	0.885/<0.001	0.224/<0.001	0.177<0.001	0.130/<0.01
BMI		1.00	0.286/<0.001	0.181/<0.001	0.133/0.003
FIQR			1.00	0.584/<0.001	0.660/<0.001
BDI				1.00	0.640/<0.001
CSI					1.00

We examined our cohort based on presence or absence of self-reported migraines. Migraine presence or absence was reported through the CSI. Based on this report, the migraine or no migraine groups were assessed for differences by weight, BMI, FIQR, BDI and CSI total scores. Migraine group weight was 87.8±27.0 with a BMI of 33.0±9.3, FIQR was 58.1±19.6. BDI was 20.8±11.2 and CSI was 63.7±16.2. No migraine group weight was 83.5±25.8 with a BMI of 30.4±11.9, FIQR was 47.6±20.8. BDI was 14.7±10.5 and CSI was 46.7±21.4. The differences between FIQR, BDI and CSI between groups was statistically significant at the <0.001 level with lower values noted in the no migraine group.

Table 4. Migraine and no migraine subjects. Values expressed as Mean +/- sd; N=number of subjects, Weight kgs, BMI: body mass index, FIQR: Fibromyalgia impact questionnaire revised, BDI: Beck depression index, CSI: Central Sensitization Inventory, Statistical significance by one tailed t test $p < 0.05$.

	Migraines	No Migraines	p-value
N	371	361	
Weight	87.8±27.0	83.5±25.8	
BMI	33.0±59.3	30.4±11.9	
FIQR	58.1±19.6	47.6±20.8	<0.001*
BDI	20.8±11.2	14.7±10.5	<0.001*
CSI	63.7±16.2	46.7±21.4	<0.001*

The CSI provides subjects the opportunity to further characterize their headaches symptoms by frequency. The rating scale is never, rarely, sometimes, often and always. Table 5 provides a breakdown of BMI, Wt, FIQR, BDI and CSI based on this rating scale and contrasts the results from the reported migraine group and the group reporting no migraine by history. Statistical significance by t test is assessed by comparing survey values in the Never or Rarely group to the Always headache group. Statistical significance for FIQR, BDI and CSI is noted by two tailed t test $p<0.001$ for both the migraine and no migraine groups.

Table 5. Migraine and no migraine subjects. Values expressed as Mean +/- sd; N=number of subjects, Weight kgs, BMI: body mass index, FIQR: Fibromyalgia impact questionnaire revised, BDI: Beck depression index, CSI: Central Sensitization Inventory, Statistical significance by two tailed t test $p < 0.001$.

	Never	Rarely	Sometimes	Often	Always
No Migraine					
N	70	106	101	61	20
BMI	27.7±8.2	30.7±16.6	30.4±9.6	31.5±9.2	33.7±8.1
Weight	80.2±26.4	82.7±25.6	84.6±25.3	84.4±27.1	89.7±29.6
FIQR	35.5±22.8	43.0±19.7	49.1±19.7	51.4±18.2	68.1±19.1*
BDI	7.5±7.7	13.9±10.0	16.5±9.6	18.4±10.5	23.8±11.6*
CSI	24.4±18.4	43.8±18.6	52.3±16.0	58.5±13.4	75.7±13.9*
Migraine					
N		20	95	164	89
BMI		30.2±8.5	35.0±9.7	32.2±8.8	33.0±9.6
Weight		81.1±23.2	94.9±27.3	87.5±26.5	90.1±27.6
FIQR		43.7±18.9	49.6±20.7	59.4±17.6	67.0±17.3*
BDI		14.3±8.8	17.4±10.4	20.9±10.1	25.8±12.3*
CSI		49.0±14.9	54.3±15.9	64.5±12.6	75.9±13.7*

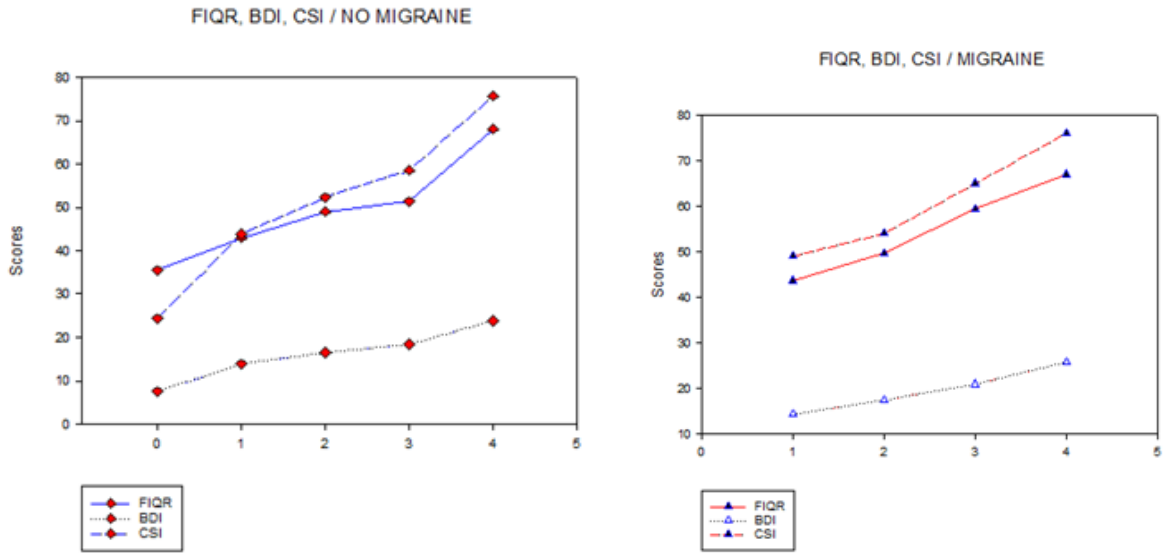

Figure 1. Positive correlations with increased frequency of headaches. Self-reported frequency of headaches displayed on x axis. 0 = never, 1 = rarely, 2= sometimes, 3= often, 4= always. Y axis displays absolute score values. Plots are for FIQR, BDI and CSI. FIQR: Fibromyalgia impact questionnaire revised, BDI: Beck depression index, CSI: Central Sensitization Inventory,

The FIQR, CSI and BDI scores showed a steady increase in values correlating with the increase in reported history of headache in our study population. A comparison of the lowest values for FIQR, BDI and CSI (scores in the Never column in Table 5 of the no migraine group compared to the scores in the Always column of the no migraine group was statistically significant at $p<0.001$ level by two tailed testing. Similarly, the FIQR, CSI and BDI scores showed a steady increase in values correlating with the increase in reported history of headache in the migraine group. A comparison of the lowest values for FIQR, BDI and CSI (scores in the rarely column in Table 5 of the migraine group

compared to the scores in the Always column of the no migraine group was statistically significant at $p<0.001$ level by two tailed testing.

3.4. ROLE OF OBESITY ON SURVEY RESPONSES

To understand the role of obesity on pain scores, we examined our cohort based on BMI. BMI ranges were designated as follows: <18.5 – Underweight, 18.5 to 25 – Normal, 25 to 30 – Overweight, 31 to 35 – Class 1 Obese, 36 to 40 – Class 2 Obese, > 40 – Class 3 Obese. Values obtained for FIQR, BDI, and CSI are depicted in Table 6. ANOVA models for FIQR, CSI, and BDI, were run. The results are reported below. Underweight values were n of 14, FIQR, BDI, and CSI, values were 50.6±16.6, 20.6±10.6, and 63.5±16.0, respectively. For BMI range 18.5-25-(Normal) n was 139, and FIQR, BDI, CSI values of 42.6±19.2, 16.4±8.8, and 57.4±15.3, respectively. For BMI range 25-30 (Overweight), n was 169, and FIQR, BDI, and CSI values of 52.8±18.9, 19.7±10.0, 60.6±14.9 respectively. For BMI range 31-35 (Class 1 Obese), n was 113, and FIQR, BDI, and CSI values of 55.5±20.0, 21.9±11.0, 63.3±16.3 respectively. For BMI range 36-40 (Class 2 Obese), n was 64, and FIQR, BDI, and CSI values of 61.1±16.8, 21.8±10.9, and 62.2±16.1, respectively. For BMI range >40 (Class 3 Obese), n was 102 and FIQR, BDI, and CSI, values of 59.7±19.2, 21.3±12.1, and 64.0±14.5 respectively.

Table 6. Clinical characteristics of BMI by Subclasses. Values expressed as Mean +/- sd; N=number of subjects, N: number of subjects, Age (range). Weight, BMI: body mass index, FIQR: Fibromyalgia impact questionnaire revised, BDI: Beck depression index, CSI: Central Sensitization Inventory, *Statistical significance by t test $p < 0.05$.

BMI Range	Designation	Meaning	(n)	FIQR	BDI	CSI
<18.5	1	Underweight	14	50.6±16.6	20.6±10.6	63.5±16.0
18.5-25	2	Normal	139	42.6±19.2	16.4±8.8	57.4±15.3
25-30	3	Overweight	169	52.8±18.9	19.7±10.0	60.6±14.9
31-35	4	Class 1 Obese	113	55.5±20.0	21.9±11.0	63.3±16.3
36-40	5	Class 2 Obese	64	61.1±16.8	21.8±10.9	62.2±16.1
>40	6	Class 3 Obese	102	59.7±19.2	21.3±12.1	64.0±14.5

A comparison of all survey values was conducted using one tailed T tests to compare survey responses between normal BMI range subjects and subjects in the underweight, overweight or obese classifications. The results of that analysis are shown in Table 7. None of the comparators of normal to underweight classification were significant. When comparing survey responses of overweight and obese patients to normal weight patients, all response values were significantly different except CSI for the overweight category which appeared to approach significance ($p=0.057$).

Table 7. P values comparing Normal BMI survey values versus other obesity ranges for each survey measure. N: number of subjects, FIQR: Fibromyalgia impact questionnaire revised, BDI: Beck depression index, CSI: Central Sensitization Inventory. * Statistical significance by t test $p < 0.05$.

BMI Range	Designation	Meaning	(n)	FIQR	BDI	CSI
<18.5	1	Underweight	14	0.084	0.169	0.098
18.5-25	2	Normal	139			
25-30	3	Overweight	169	<0.001*	0.007*	0.057
31-35	4	Class 1 Obese	113	<0.001*	<0.001*	0.004*
36-40	5	Class 2 Obese	64	<0.001*	0.002*	0.031*
>40	6	Class 3 Obese	102	<0.001*	0.005*	0.001*

3.5. IMPACT OF MEDICATIONS ON SURVEY RESPONSES

To understand the role of medication impact on survey scores, we examined survey responses in a cohort of subjects with FM who were on no prescription medication and contrasted them to a larger sample that was on prescription medications. Values obtained for FIQR, BDI, and CSI, are depicted in Table 8. ANOVA models for age, range, weight, FIQR, CSI, and BDI, were run. The results are reported below. Values for the Non-Medicated group showed an n of 64, a range of 19-78 years and values for Wt, BMI, FIQR, BDI, and CSI, of 86.3±28.3, 30.9±8.6, 48.6±23.4, 18.9±11.6, 60.2±16.8, respectively. For FM subjects on medications the values were n of 598, age range of 18-76, and values for Wt, BMI, FIQR, BDI, and CSI, of 86.8±26.1, 31.9±9.2, 53.9±19.4, 20.3±10.7, 61.8±14.8. The only significant difference between the two groups was noted with a lower age in the non-medicated group ($p+=0.024$).

Table 8. Clinical characteristics of FM on no medications versus FM on Medications. Values expressed as Mean +/- sd; N=number of subjects, N: number of subjects, Age (range). Weight, BMI: body mass index, FIQR: Fibromyalgia impact questionnaire revised, BDI: Beck depression index, CSI: Central Sensitization Inventory. * Statistical significance by t test $p < 0.05$.

	FM – No Meds	FM – On Meds	p value
N	64	598	
Age	40.0±13.0	43.9±14.1	0.024*
Range	19-78	18-76	
Weight	86.3±28.3	86.8±26.1	0.623
BMI	30.9±8.6	31.9±9.2	0.492
FIQR	48.6±23.4	53.9±19.4	0.103
BDI	18.9±11.6	20.3±10.7	0.213
CSI	60.2±16.8	61.8±14.8	0.571

Discussion

Fibromyalgia is a chronic debilitating condition that contributes significantly to overall expenditures on health care globally. In addition to increased per capita costs per individual, there is a significant burden on society in terms of decreased work productivity and impaired family relationships due to lack of understanding of the degree to which an individual family member might be "compromised" by this disease that superficially shows no obvious signs of injury or impairment [43]. Due to the nature of this condition and its societal impact as well as the lack of readily available objective biomarkers needed for diagnosis and assessment of this condition, proper identification of distinct clinical phenotypes might lead to earlier intervention particularly from the standpoint of more effective treatments and diminished physical and psychological impact on the affected individual. Fibromyalgia can produce systemic complaints that can confound the practitioner and frustrate the patient. In addition, the numerous complaints are often not ameliorated by a single therapeutic approach. Therefore, treatment needs to be targeted to clinical domains of "illness" in order to achieve positive therapeutic outcomes. For example, if patients were to complain of profound dysesthesias, then classes of medications like voltage gated calcium modulators might be appropriate (e.g. pregabalin). Alternatively, serotonin and norepinephrine reuptake inhibitors (SNRI) such as duloxetine or milnacipran might be first line options for symptoms of cognitive impairment. As reflected in our analyses, early targeting of headache and in specific, minimizing the frequency or chronification of headache might provide amelioration of the overall impact of FM as reflected by the FIQR. Similarly, a reduced CSI might also lead to diminished global central sensitization symptoms and subsequent improvement in quality of life. Therefore, headache and migraine clearly adversely affect global FM QOL. Similarly, obesity has been previously shown to be a major detriment to overall FM QOL and is seen in our study population as well.

The results of our analyses are intriguing. As expected, a general comparison of male and female subject responses yielded a female predominance of enrollees at a level of 13:1; higher than the typical levels seen in these studies but consistent with the overall increased frequency of FM in female relative to male subjects. As shown in Table 1, statistically significant levels were seen in F:M with higher values noted for F for weight, BMI, and FIQR. There were no other statistically significant differences between the groups. Although the male values are low considering the ratio of F:M, these findings are consistent with prior studies and therefore are unlikely to be due to generalization error. Our findings are also consistent with the recent findings of Favretti and colleagues comparing gender differences between males and females with regard to the revised FIQR despite our cohort having a larger subject number[44].

All the questionnaire surveys yielded positive Pearson correlation studies as noted in Table 3. Pearson correlation paired analyses showed that the strongest positive correlations were between the following pairs: Wt-BMI (0.885), FIQR-CSI (0.660), CSI-BDI (0.640), and FIQR-BDI (0.584). Some of these correlations such as weight and BMI are obvious as these parameters have been previously shown to be strong predictors of pain [35-40]. Similarly, strong correlations between CSI and BDI are seen probably due to shared measurable elements between all these survey tools (e.g. pain in FIQR and CSI, etc.). These findings are further supported by reports of increased anxiety in individuals with high pain levels which are reflected in higher CSI levels [45]

Presence and absence of migraines was strongly associated with concurrent presence or absence of depression, higher FIQR and CSI as noted in Table 4. These findings are consistent with previous

reports [46]. Table 5 and Figure 1 show greater detail of the CSI data and support the notion that with increased frequency/chronicity, symptoms in the FM cohort become further exacerbated. These findings are supported by previous literature and are an argument for early intervention of migraines in this population [21,23-25].

Weight class and body mass index analyses are shown in Table 6 and Table 7. Our findings show that in comparing normal BMI to elevated BMI levels, there are statistically significant increases in FIQR, BDI and CSI whenever the BMI is above normal range. This indicates that BMI is a major driver of survey responses and contributes significantly to a decrease in quality of life. Our findings are consistent with numerous studies attesting to the significance of weight in worsening overall symptoms of FM [47-53]. The small n noted in the underweight class did not allow us to draw any conclusion about whether underweight classes may also have some level of impact on survey responses.

Fibromyalgia patients are well known to have a high medication burden [54]. Previous studies have reported on the number of medications from varied classes that affected individuals are on and have also shown the wide variety of specialties that prescribe for FM patients. We had surmised that FM subjects who were on no medications might be a subgroup that would display significantly lower burden of disease as reflected by lower FIQR, CSI and/or BDI. Surprisingly, we found that there were no statistically significant differences in survey responses for individuals with FM on medication relative to those not on medication as noted in Table 8. Despite the unequal n's of the groups, sample sizes are not one of the assumptions made in a t test. In that, the age, range, weight, BMI, BDI and CSI were similar suggest that at least for our university cohort, number of medications was not an important factor in determining whether patients had a higher FIQR level or not.

Conclusions

This survey of a large cohort of subject with FM is insightful. Headache and migraine frequency adversely impact FM quality of life. There is a positive correlation between presence and frequency of headaches and increased symptoms of central sensitization as reflected by increased CSI scores. An increased headache frequency correlates with higher levels of depression as assessed by the BDI. Obesity is also a major factor contributing to FM impact, increased CSI scores and increased depression as assessed by the BDI. In contrast, segregating FM patients by whether they are on prescription medications or not prior to survey completion does not appear to be a factor that correlates with FM survey responses. A multi-dimensional approach to treatment of FM has long been recognized and is emphasized with the findings of this study. Headaches including migraine control and BMI should be prime treatment targets to prevent worsening of a variety of quality of life measures in FM patients. A better understanding of the overall categories of FM determinants in terms of quality of life can help to design and prioritize targeted treatments for these individuals.

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