RESEARCH ARTICLE

The oracle study — fibromyalgia, prevalence and severity in the hospital setting in the Pakistani population

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Abstract

Objective: To assess the prevalence and severity of fibromyalgia in hospital-visiting patients.

Methods: The cross-sectional study was conducted at the Pakistan Institute of Medical Sciences, Islamabad, Pakistan, from July, 2018, to January, 2019, and comprised patients aged 18-75 years of either gender. Demographic information, comorbidities and previous medications were recorded for each patient. The modified American College of Rheumatology preliminary diagnostic criteria 2010-11 for fibromyalgia diagnosis. If diagnosed, the fibromyalgia impact questionnaire was administered to assess its severity. Data was analysed using SPSS 25.

Results: Of the 750 hospital-visiting patients, fibromyalgia was diagnosed in 250(33.3%); 190(76%) of them being females ($p<0.0001$). Comorbidities, age and increased elevated body mass index were significantly associated with fibromyalgia. Severity was not influenced by comorbidities, marital status, education or economic status ($p>0.05$). Menarche at a later age and menstrual irregularity were associated with fibromyalgia severity ($p<0.05$).

Conclusion: The hospital-based prevalence of fibromyalgia was found to be high, especially among females.

Keywords: Fibromyalgia, Chronic widespread pain, Prevalence, Hospital setting, Pakistan. (JPMA 71: 1357; 2021)

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Introduction

Fibromyalgia syndrome (FMS) has remained an enigma over the years. The first mention of the syndrome appeared in literature over a century ago, with the first official diagnostic guidelines being published by the American College of Rheumatology (ACR) in 1990.[1] The diagnosis has often been contested, with its acceptance in clinical literature becoming more gradually marked over the last three decades. It remains a diagnostic challenge due to the considerable overlap in clinical features and absence of specific laboratory investigations. The disease has been surrounded by controversy regarding both its diagnosis and management, and, despite the considerable impact on patients as a result of the condition, no medical specialty has yet laid claim to the syndrome. The ACR revisited the diagnosis, and published the revised ACR 2010 preliminary diagnostic criteria.[2] Further revisions were undertaken in 2016, the most significant of which was published by Wolfe et al.,[3] stating that FM diagnosis is valid irrespective of other diagnoses, and an FM diagnosis does not exclude the presence of other clinically important diseases.

The hallmark of FM is chronic widespread pain, the origins of which have been proposed to be neurogenic in origin. It has been postulated that a central, amplified pain perception is linked with allodynia and hyperalgesia. Other components of the syndrome include fatigue, sleep disturbances, generalised tenderness and cognitive difficulties, the latter being referred to as 'fibro fog'.[4] Despite the diverse and wide-ranging nature of symptoms, FM may be considered a discrete diagnosis or a constellation of clinical features. The essential aspect that warrants mention is that effective treatment for FM, both pharmacological and non-pharmacological, is now possible.[5]

Population-based epidemiological studies in the United States have estimated an FM prevalence of 2-4%, with levels rising to 15% in patients presenting to rheumatology clinics.[6] Epidemiological data is scarce in the Asian region. The current study was planned to assess FM prevalence in the hospital setting in a cross-section of Pakistani population, and to assess FM severity.

Patients and Methods

This cross-sectional study was conducted from July, 2018, to January, 2019, at the Pakistan Institute of Medical Sciences (PIMS), which is the largest tertiary care hospital in Islamabad, catering to patients from all over Pakistan. After approval from the institutional ethics review committee, the sample size was calculated using the World Health Organisation (WHO) calculator[7] while setting the confidence level at 99%, margin of error at 5% and the reported hospital prevalence of FM up to 36%.[8] The sample was raised using convenience sampling technique from among patients visiting different

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Annexure: Data-collection tool.

DEPARTMENT OF INTERNAL MEDICINE – UNIT 1

THE ORACLE STUDY

DEMOGRAPHIC DATA								Date	
Administering Doctor									
Patient Name									
Sex	☐ Male	☐ Female	Age		Ht.		Wt.		
PCN:							Tel:		

Marital Status:	☐ Married	Education:	☐ Uneducated
	☐ Unmarried		☐ Primary
	☐ Widowed		☐ Secondary
	☐ Divorced		☐ Intermediate
Monthly Income	☐ <20,000		☐ Graduate
	☐ 20,000-40,000	Most Relevant Problem (Please tick)	
	☐ >40,000	Pain درد	Fatigue تھکان Lethargy سستی

Comorbidities (Please circle)					
DM	HTN	RA	SLE	Unrefreshing sleep نیند لینے کے باوجود سستی کا رہنا	Cognitive Symptoms یاد داشت کی کمزوری یا سوچنے میں مسائل
IHD	Depression	Hypothyroidism			

Have you ever visited a doctor for your complaints, If yes, please mention where:	
Never sought Medical help	☐
Primary care/GP	☐
Secondary Care/ Hospital	☐
Tertiary Care	☐

FIBROMYALGIA DIAGNOSIS

1. WIDESPREAD PAIN INDEX (WPI)

In the past week, where have you experienced **pain**? Please tick all boxes that apply

گزشتہ ایک ہفتے کے دوران آپکو کہاں کہاں درد ہوا ہے؟

Left Upper Region ☐	**Right Upper Region** ☐	**Axial Region** ☐	**Left Lower Region** ☐	**Right Lower Region** ☐
☐ Lt. Jaw باٹیاں جبڑا	☐ Rt. Jaw داٹیاں جبڑا	☐ Neck گردن	☐ Lt. hip باٹیاں کولھا	☐ Rt. Hip داٹیاں کولھا
☐ Lt. Shoulder Girdle باٹیاں کاندھا	☐ Rt. Shoulder Girdle داٹیاں کاندھا	☐ Upper Back کمر کا اوپر کا حصہ	☐ Lt. Thigh باٹیں ٹانگ	☐ Rt. Thigh داٹیں ٹانگ
☐ Lt. Upper Arm باٹیاں بازو	☐ Rt. Upper Arm داٹیاں بازو	☐ Lower Back کمر کا نچلا حصہ	☐ Lt. Leg باٹیں پنڈلی	☐ Rt. Leg داٹیں پنڈلی
☐ Lt. Lower Arm باٹیاں بازو (کہنی اور کلائی کے درمیان)	☐ Rt. Lower Arm داٹیاں بازو (کہنی اور کلائی کے درمیان)	☐ Chest چھاتی/سینا		
		☐ Abdomen پیٹ		

Total WPI Score (Boxes other than regions) [0-19]: _____

Total Number of Regions ticked [Max 5]: _____

2. SYMPTOM SEVERITY SCORE

For each of the following symptoms, please tick according to **severity**

	0 = No Problem کوئی مسئلہ نہیں	1 = Slight or mild problem, often mild or intermittent تھوڑا سا مسئلہ، ہلکا پھلکا، وقتے وقتے سے	2 = Moderate, considerable problem, often present کافی حد تک مسئلہ، اکثر تکلیف کا سبب	3 = Severe, pervasive, continuous, life-disturbing شدید مسئلہ، لگاتار، زندگی متاثر ہو جاتی ہے
Fatigue تھکنا/کمزوری کا احساس				
Waking Unrefreshed سونے کے بعد بھی تھکے ہوئے جاگنا				
Cognitive Symptoms یاد داشت کی کمزوری یا سوچنے میں مسائل				

In the past week, have you been bothered by any of the following?

گزشتہ ہفتے کے دوران کیا ان میں سے کوئی تکلیف ہوئی ہے؟

	0 = No problem کوئی مسئلہ نہیں	1 = Problem مسئلہ ہے
Headaches سر میں درد	☐	☐
Pain or cramps in lower abdomen پیٹ میں درد یا مروڑ	☐	☐
Depression غمگین ہونا	☐	☐

Total SS Score (Add all numbers) [0-12]: _____

FIBROMYALGIA DIAGNOSIS

SUMMARY/DIAGNOSIS

☐ **1. Criteria I: WPI ≥ 7 and SSS ≥ 5 OR**
WPI 4-6 and SSS ≥ 9

☐ **2. Generalized Pain (4 out of 5 pain regions selected)**

☐ **3. Symptoms present for ≥ 3 months**

FIBROMYALGIA DIAGNOSED?

YES

NO

ASSESSING THE SEVERITY OF FIBROMYALGIA – THE REVISED FIBROMYALGIA IMPACT QUESTIONNAIRE

There are **three** domains in this questionnaire. The first domain measures patient **function** status, the second measures the **overall impact** of fibromyalgia and the third measures intensity of **symptoms.**

Patients are asked to score the question on a scale of 0 to 10.

I. FUNCTION DOMAIN/ACTIVITY LEVEL

Directions:

For each of the following 9 questions, check the box that best indicates how much your Fibromyalgia made it difficult to perform each of the following activities during the past 7 days. If you did not perform a particular activity in the last 7 days, rate the difficulty for the last time you performed the activity. If you can't perform an activity, check the last box.

نیچے دیئے ہوئیے9 سوال ہیں۔ گزشتہ ایک ہفتے کے دوران آپکی تکلیف کی وجہ سے ان کاموں میں آپکو کتنا مسئلہ ہوا ہے؟ اگر گزشتہ ایک ہفتے میں ان میں سے کوئی کام نہیں کیے تو جب آخری مرتبہ کیے تھے تو کتنا مسئلہ ہوا تھا؟ اگر ان میں سے کوئی بھی کام آپ سے نہیں ہو پاتا تو 10 نمبر دیجیے

Brush or Comb your Hair بالوں میں کنگھی کرنا	**No Difficulty** کوئی مشکل نہیں	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10	**Very Difficult** بہت مشکل ہے
Walk Continuously for 20 minutes 20 منٹ لگاتار پیدل چلنا	**No Difficulty** کوئی مشکل نہیں	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10	**Very Difficult** بہت مشکل ہے
Prepare a homemade meal گھر میں کھانا پکانا	**No Difficulty** کوئی مشکل نہیں	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10	**Very Difficult** بہت مشکل ہے
Vacuum, scrub or sweep floors گھر کے فرش کو صاف کرنا، پوچھا لگانا	**No Difficulty** کوئی مشکل نہیں	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10	**Very Difficult** بہت مشکل ہے
Lift and carry a bag full of groceries گھر کے سودے کے لفافے کو اٹھانا اور لے کر جانا	**No Difficulty** کوئی مشکل نہیں	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10	**Very Difficult** بہت مشکل ہے
Climb one flight of stairs ایک منزل سیڑھیاں چڑھنا	**No Difficulty** کوئی مشکل نہیں	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10	**Very Difficult** بہت مشکل ہے
Change bed sheets بستر کی چادر بدلنا	**No Difficulty** کوئی مشکل نہیں	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10	**Very Difficult** بہت مشکل ہے
Sit in a chair for 45 minutes کرسی پر 45 منٹ بیٹھنا	**No Difficulty** کوئی مشکل نہیں	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10	**Very Difficult** بہت مشکل ہے
Go Shopping for groceries گھر کے سودے کے لئے بازار سے خریداری کرنے جانا	**No Difficulty** کوئی مشکل نہیں	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10	**Very Difficult** بہت مشکل ہے

Add the scores for the 9 questions above in Section I and write your Sub-total score below. Then divide this number by 3 (three) to determine your Adjusted sub-total score. Write this number below.

SUBTOTAL SCORE DOMAIN I: _____

ADJUSTED SUBTOTAL SCORE (divide the number above by 3): _____

II. OVERALL IMPACT

Directions:

For each of the following 2 questions, check the box that best describes the overall impact of your fibromyalgia over the last 7 days.

نیچے دیئے 2 سوال ہیں۔ گزشتہ ایک ہفتے کے دوران آپکی تکلیف کی وجہ سے مجموعی طور پر کتنا مسئلہ ہوا؟

Fibromyalgia prevented me from accomplishing goals for the week میری تکلیف کی وجہ سے مجھے ہفتے کے کام پورے کرنے میں ناکامی ہوئی	**Never**	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ 0 1 2 3 4 5 6 7 8 9 10	**Always**
I was completely overwhelmed by my fibromyalgia symptoms مجھے میری تکلیف نے بے بس کر دیا	**Never**	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ 0 1 2 3 4 5 6 7 8 9 10	**Always**

SUBTOTAL SCORE DOMAIN II: _____

III. INTENSITY OF SYMPTOMS

For each of the following 10 questions, select the box that best indicates your intensity of these common fibromyalgia symptoms over the past 7 days

نیچے دیے ہوئے 10 تکالیف آپکو کتنی شدت سے محسوس ہوتی ہیں؟

Please rate your level of pain آپکو درد کس شدت سے ہوتا ہے	**No Pain** کوئی درد نہیں	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ 0 1 2 3 4 5 6 7 8 9 10	**Unbearable Pain** برداشت سے باہر درد
Please rate your level of energy بدن میں طاقت کتنی محسوس کرتے ہیں	**Lots of Energy** بہت طاقت	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ 0 1 2 3 4 5 6 7 8 9 10	**No Energy** کوئی طاقت ہی نہیں
Please rate your level of stiffness بدن کتنا اکڑتا ہے	**No Stiffness** کوئی اکڑا ہٹ نہیں	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ 0 1 2 3 4 5 6 7 8 9 10	**Severe Stiffness** بہت شدید اکڑا ہٹ
Please rate the quality of your sleep آپکو نیند کیسی آتی ہے	**Awoke well rested** اٹھنے کے بعد تازہ	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ 0 1 2 3 4 5 6 7 8 9 10	**Awoke very tired** اٹھنے کے بعد تھکان

IINITIAL VISIT

Please rate your level of Depression آپ کتنا غمگین محسوس کرتے ہیں	**No Depression** کوئی غم نہیں	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10	**Very Depressed** بہت غمگین
Please rate your level of memory problems آپ کی یاد داشت کیسی ہے	**Good Memory** یاد داشت اچھی ہے	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10	**Very Poor Memory** بہت کمزور یاد داشت ہے
Please rate your level of Anxiety گھبراہٹ کتنی محسوس کرتے ہیں	**Not Anxious** کوئی گھبراہٹ نہیں	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10	**Very Anxious** بہت زیادہ گھبراہٹ
Please rate your level of tenderness to touch بدن دبانے سے کتنا درد ہوتا ہے	**No Tenderness** کوئی درد نہیں	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10	**Very Tender** بہت درد ہوتا ہے
Please rate your level of balance problems کھڑے ہوتے یا چلتے ہوئے یا آپ گرنے والے ہوتے ہیں؟	**No Imbalance** کوئی چکر نہیں آتے، کبھی نہیں گرتے	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10	**Severe Imbalance** کافی چکر آتے ہیں، اکثر گرنے کا ڈر ہوتا ہے
Please rate your level of sensitivity to loud noises, bright lights, odours and cold کس حد تک آپ کو شور، تیز روشنی، بو یا سردی سے مسئلہ ہوتا ہے؟	**No Sensitivity** کوئی مسئلہ نہیں	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10	**Extreme Sensitivity** بہت شدید مسئلہ

SUBTOTAL SCORE FOR DOMAIN III: _____

ADJUSTED SUBTOTAL SCORE (divide the number above by 2)**: _____Total**

FIQR SCORING

INDIVIDUAL DOMAINS:

1. FUNCTION/ACTIVITY: _____
2. OVERALL IMPACT: _____
3. INTENSITY: _____

TOTAL FIQ Score: _____

INTERPRETING SEVERITY OF SYMPTOMS (Please tick relevant box)

- ☐ **Mild FM (Total score 0 – 42)**
- ☐ **Moderate FM (Total score 43 – 59)**
- ☐ **Severe FM (Total score 60 – 74)**
- ☐ **Extreme FM (Total Score 75 – 100)**

departments of the hospital. Those included were patients of either gender aged 18 years and above. Those excluded were patients on treatment for clinical depression and those who could not comprehend the questionnaire secondary to mental illness. Data was collected after taking written informed consent from each participant.

The administered questionnaire had three sections (Annexure). The first part dealt with patients' demographic data, including age, gender, marital status, education status, height, weight, body mass index (BMI), presence of comorbid illnesses, like diabetes, hypertension, ischaemic heart disease, arthritis, hypothyroidism and chronic kidney disease, and gender-specific details about menstrual cycles,

like menarche, regularity, presence or absence of hyperandrogenism. Additionally, previous treatment, if any, for their symptoms was noted, and the extent of symptomatic improvement that they may have experienced.

The second segment consisted of the 2010-11 modified ACR preliminary diagnostic criteria for FM,[2] including the widespread pain index[9] (WPI) comprising five body regions and 19 specific parts of the body overall, and the symptoms severity score (SSS), which measures the presence and severity of fatigue, cognitive symptoms, waking unrefreshed, headaches, abdominal pain/cramps and depression. The questionnaire was translated into Urdu and was validated in a subset of 40 bilingual patients (α=0.93). FM was diagnosed if a patient had WPI ≥7 with SSS ≥5, or WPI 4-6 and SSS ≥9, generalized pain, defined as involvement of 4 out of 5 regions, and persistence of symptoms for ≥3 months.

The third section measured FM severity using the Fibromyalgia Impact Questionnaire (FIQR) 2019 version,[10] which is divided into three domains, measuring function, overall impact and symptom intensity. The physical functional domain has 9 questions, the overall impact domain has 2 questions, and the symptom severity domain has 10 items. Each of the 21 items is scored 1-10. Adjusted domain scores were calculated by adding half of the functional domain, the complete overall impact domain and one-third of the symptom intensity domain, thus giving a score out of 100. The adjusted individual domain scores were added and the severity of symptoms was graded according to the final score. The corresponding scores were considered as mild (score 0-42), moderate (43-59), severe (60-74) or extreme (75-100). The FIQR was translated into Urdu as well, and was validated before use in the study in a subset of 54 patients who were fluent in both English and Urdu (α=0.89).

Data was analysed using SPSS 25, and it was found to be normally distributed. Demographic and clinical parameters were measured using descriptive statistics and their statistical significance was measured by chi-square test. Differences in gender were further assessed by using binary logistic regression to calculate the odds ratio (OR). Continuous variables were analysed using analysis of variance (ANOVA). Multiple regression analysis was used to determine the factors affecting FM severity. The presence of correlation was determined with Pearson's correlation coefficient. P<0.05 was taken as statistically significant.

Results

Of the 767 patients enrolled, 750(97.7%) completed the

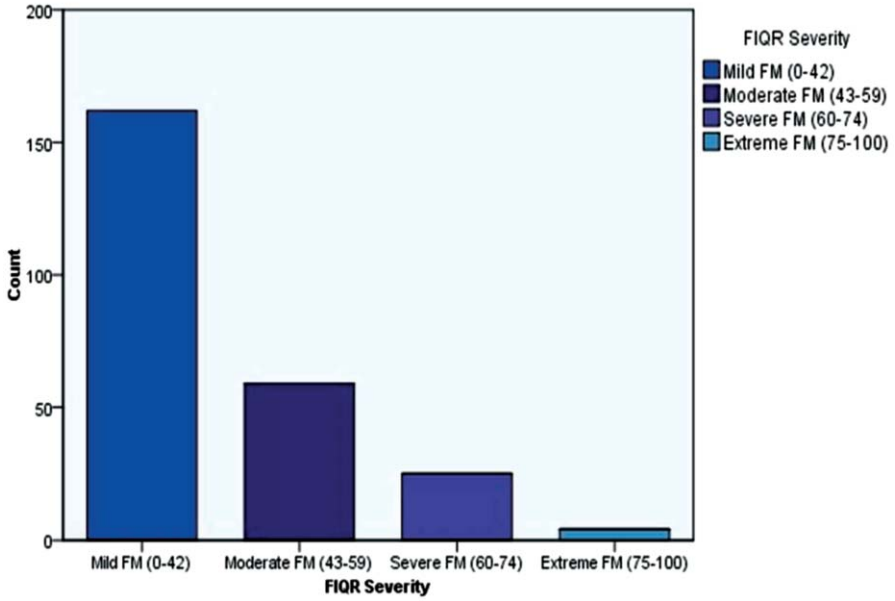
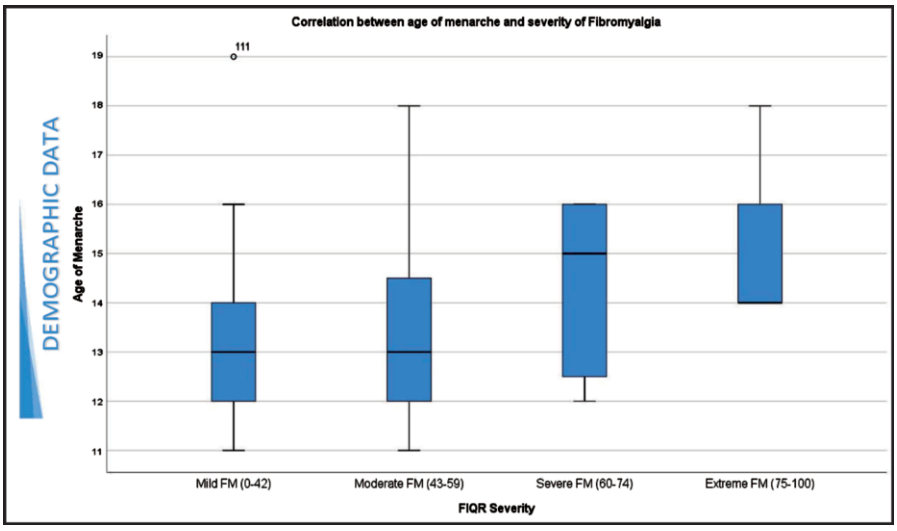


Figure-1: Severity of fibromyalgia as measured by revised fibromyalgia impact questionnaire.



FIQR- Fibromyalgia Impact Questionnaire. FM- Fibromyalgia

Figure-2: Correlation between age of menarche and severity of fibromyalgia.

Table-1: Demographic characteristics of study population.

		Count	Percentage	Mean	95% CI	Standard Deviation
Gender	Male	298	39.7%			
	Female	452	60.3%			
Age				42	41 - 43	16
Age Group	< 20 Years	76	10.1%			
	20 - 30 Years	141	18.8%			
	31 - 40 years	145	19.3%			
	41 - 50 Years	175	23.3%			
	51 - 60 Years	101	13.5%			
	61 - 70 Years	89	11.9%			
	>70 Years	23	3.1%			
BMI				24.6	24.1-25.1	5.5
Marital Status	Married	563	75.1%			
	Unmarried	153	20.4%			
	Widowed	28	3.7%			
	Divorced	6	0.8%			
Educational Status	Uneducated	217	28.9%			
	Primary	228	30.4%			
	Secondary	138	18.4%			
	Intermediate	83	11.1%			
	Graduate	84	11.2%			
Monthly Income	< PKR 20,000	356	47.5%			
	PKR 20,000 - 40,000	317	42.3%			
	> PKR 40,000	77	10.3%			
Comorbidities	None	164	21.9%			
	Diabetes	256	34.1%			
	Hypertension	126	16.8%			
	Ischaemic Heart Disease	16	2.1%			
	Chronic Kidney Disease	3	0.4%			
	Anaemia	79	10.5%			
	Anxiety	62	8.3%			
	Rheumatoid Arthritis	9	1.2%			
	SLE	5	0.7%			
	Hypothyroidism	8	1.1%			
	Osteoarthritis	22	2.9%			

CI: Confidence interval; BMI: Body mass index; PKR: Pak rupee; SLE: Systemic lupus erythematosus.

questionnaire 452(60.3%) females and 298(39.7%) males. The overall mean age was 42.2±16 years, with 537(71.6%) aged <50 years. The overall mean BMI was 24.6±5.5kg/m^2 (Table-1).

FM was found in 250(33.3%) patients; 190(76%) females, 60(24%) males (p<0.0001). Diabetes, anxiety and rheumatoid arthritis, advancing age and increased BMI were significantly associated with FM presence (Table-2).

Further, 196(78.4%) patients reported pain as their most relevant problem, with fatigue/lethargy being reported by 49(19.6%). Unrefreshing sleep and was highlighted by 4(1.6%) patients and cognitive problems by 1(0.4%). Also, 180(70%) patients had musculoskeletal pain and had received multiple courses of non-steroidal anti-inflammatory drugs (NSAIDs), with 165(66%) being on long-term NSAID therapy exceeding 6 months.

The mean FIQR score was 37.17 (95% CI: 34.99-39.29) with 162(64.8%) having mild FM (Figure-1).

FM severity was not influenced by the presence of co-morbidities, marital status, level of education or economic status (p>0.05). The most relevant problem, as reported by the patient, also had no significant impact on FM severity (p>0.05). A unique finding was a small but significant correlation between the age of menarche (p=0.009) and irregularity of menstrual cycles (p=0.003) and FM intensity, with a later age of menarche and cyclical irregularity being associated with more severe FM symptoms (Figure-2). No such correlation was observed when clinical features of androgen excess were analysed (p>0.05).

Table-2: Association of fibromyalgia diagnosis with the explored factors.

		Fibromyalgia Diagnosed				Fibromyalgia not diagnosed				
		Count	Percentage	Mean ± SD	95% CI for Mean	Count	Percentage	Mean ± SD	95% CI for Mean	p-value
Gender	Male	60	24.0%			238	47.6%			<0.0001*
	Female	190	76.0%			262	52.4%			
Age				44.7 ± 15.8	43 - 47			40.9 ± 15.7	39 - 42	0.002ǂ
Age Group	< 20 Years	14	5.6%			62	12.4%			0.044*
	20 - 30 Years	43	17.2%			98	19.6%			
	31 - 40 years	48	19.2%			97	19.4%			
	41 - 50 Years	63	25.2%			112	22.4%			
	51 - 60 Years	35	14.0%			66	13.2%			
	61 - 70 Years	36	14.4%			53	10.6%			
	>70 Years	11	4.4%			12	2.4%			
BMI				24.4 ± 6.1	23.4 - 25.3			24.6 ± 5.3	24.1 - 25.2	0.004ǂ
Marital Status	Married	194	77.6%			369	73.8%			0.562
	Unmarried	34	13.6%			119	23.8%			
	Widowed	20	8.0%			8	1.6%			
	Divorced	2	0.8%			4	0.8%			
Educational Status	Uneducated	81	32.4%			136	27.2%			0.288
	Primary	66	26.4%			162	32.4%			
	Secondary	52	20.8%			86	17.2%			
	Intermediate	29	11.6%			54	10.8%			
	Graduate	22	8.8%			62	12.4%			
Monthly Income	< PKR 20,000	125	50.0%			231	46.2%			0.641
	PKR 20,000 - 40,000	97	38.8%			220	44.0%			
	> PKR 40,000	28	11.2%			49	9.8%			
Comorbidities	None	43	17.2%			121	24.2%			
	Diabetes	104	41.6%			152	30.4%			<0.0001*
	Hypertension	40	16.0%			86	17.2%			
	Ischaemic Heart Disease	2	0.8%			14	2.8%			
	Chronic Kidney Disease	1	0.4%			2	0.4%			
	Anaemia	15	6.0%			64	12.8%			
	Anxiety	32	12.8%			30	6.0%			0.001*
	Rheumatoid Arthritis	6	2.4%			3	0.6%			0.033*
	SLE	2	0.8%			3	0.6%			
	Hypothyroidism	1	0.4%			7	1.4%			
	Osteoarthritis	4	1.6%			18	3.6%			
Age of Menarche				13.4 ± 1.6	13 -14			13.0 ± 1.2	12.8 - 13.2	0.007ǂ
Cycles Regular	Yes	134	81.2%			190	82.6%			0.721*
	No	31	18.8%			40	17.4%			

CI: Confidence interval; SD: Standard deviation; BMI: Body mass index; PKR: Pak rupee; SLE: Systemic lupus erythematosus. * χ^2 test, ǂ ANOVA (Analysis of Variance), p<0.05 taken as statistically significant.

Discussion

The presence of FM has been extensively documented alongside other clinical illnesses and its recognition provides avenues for correct management.[11] These proposed mechanisms have been summarised[12] and involve abnormal sensitisation from a peripheral nerve stimulus that could originate from deep muscle or fascia, sensitising the central nervous system (CNS) as a final pathway for FM.[13-15] This phenomenon could in turn lead to allodynia or a more acute somatosensory perception, dysregulation of the autonomic nervous system, as well as alterations in CNS physiology.[16-18] Other abnormal physiological findings have been identified and include abnormal sleep electroencephalograms, neuroendocrine perturbations, a pro-excitatory state suggested by abnormal changes in the neurochemistry of cerebrospinal fluid (CSF), cortical hyper-activation in response to both noxious and non-noxious stimuli, central dopaminergic transmission disruption and an apparent acceleration in age-associated brain atrophy that correlates with illness duration.[19-22] The observation that FM tends to aggregate in families has led to the postulation that there may be a genetic predisposition, with the

identification of several genes as possible candidates, predominantly those that involve neurotransmitter physiology.[23] The brainstem has also been implicated, with clinical studies having shown that there are alterations in excitatory and inhibitory brainstem inter-neuronal circuits signifying brainstem dysfunction.[24] It has also been hypothesised that there is maladaptive plasticity of the primary motor cortex in FM patients.[25] Recent studies have shown some evidence demonstrating that oxidative stress, mitochondrial dysfunction and inflammation may have a role in FM pathophysiology.[26]

The current study found FM rate in hospital-visiting patients to be 33.3%. The rate is lower than the 31% reported in a study comprising Turkish geriatric population.[27] The current study also found a significant increase in FM prevalence with advancing age.

The association between an increased BMI and FM merits further understanding. Our observation regarding this significant correlation mirrors a study,[28] which confirmed that the prevalence of increased body weight and obesity was high in FM, and suggested that physicians treating FM should be aware of the bivariate linear correlations and discuss weight-loss with their FM patients. Even if increasing BMI is not intrinsic to FM, it contributes to poor mood and functional outcome and should be a treatment goal. The clinical implications of this association were further explored by a study[29] which found that C-reactive protein (CRP) and apolipoprotein B, biomarkers linked to cardiovascular events may be associated with FM-related dysfunction in normal- and over-weight women with FM and that their increased levels in these patients may indicate an increased risk of cardiovascular disease.

Researchers in Turkey concluded that FM patients had a better course of illness when their education and socio-economic status were in good condition, and the complications of pain and illness were further reduced. However, the current findings did not find any significance with regards to socio-economic status or education.[30]

A unique observation of the current study is that there may be a hormonal basis to FM intensity, with menstrual irregularity and a later menarche age correlating with more severe FM symptoms in the female subset. A study[31] found that day-to-day changes in progesterone as well as testosterone were significantly and inversely correlated with pain severity. It found no relationship between estradiol and pain or cortisol and pain. The results suggest that progesterone and testosterone play a protective role in FM pain severity and that gender and other hormones may serve to increase as well as decrease FM pain severity.[31]

A study[32] using animals concluded that 17β-estradiol produced anti-hyperalgesic and antiallodynic effects 24h, but not 8h, after its administration, suggesting a genomic mechanism. It supports the FM model for searching alternatives of treatment, particularly during endocrine phases when pain is exacerbated, such as menopause, and that 17β-estradiol replacement might be useful.

Recent evidence has focussed on a possible immunological background in FM. Cytokines/chemokines, lipid mediators, oxidative stress and several plasma-derived factors underlie the inflammatory state in FM, leading to potential new therapeutic options targeting inflammatory pathways in FM patients. There is evidence to support the inflammation-driven pathways in FM pathogenesis, but further research is required to fully understand the network of inflammation and its possible role in diagnosis and/or treatment.[33]

The role of oxidative stress and the use of antioxidants also provides a window for new modalities of treatment in the future. There are several studies indicating oxidative stress in patients with FMS. Oxidant malondialdehyde and antioxidant superoxide dismutase balances were found to be changed in FMS patients. Furthermore, increased free radical levels may be responsible for the development of FMS, and free radical-mediated oxidative stress, including inflammatory cytokines, may also play important roles in its pathogenesis.[34]

To the best of our knowledge, the current study is the first of its kind conducted in the Pakistani population. It has made significant observations that can be further explored in well-designed, longitudinal, multi-centre studies.

However, the current study has limitations, like having a cross-sectional design which limits the ability to identify a causal relationship between the factors analysed, and the fact that it was a single-centre study.

Conclusion

FM prevalence was noted in about one-third of the patients visiting a hospital. Adequate understanding of the diagnostic criteria, and the availability of treatment modalities could enable physicians from all disciplines to correctly manage the disorder. Incorrect management approaches, such as the indiscriminate use of NSAIDs, can only be corrected if the disorder is correctly diagnosed.

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