RESEARCH ARTICLE

FIBROMYALGIA IN HEPATITIS C PATIENTS; A CROSS-SECTIONAL STUDY FROM PAKISTAN

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ABSTRACT

Fibromyalgia syndrome (FS) is a chronic musculoskeletal illness involving anatomic locations of tender points and discomfort at certain levels. The study was carried out to ascertain the prevalence of hepatitis C virus Infection in Fibromyalgia Patients.

Methodology: *This cross-sectional descriptive study was conducted at the Mayo Hospital Lahore from 1st January to 30th May 2019. The patients who presented to Mayo Hospital Lahore with hepatitis C virus infection throughout the research period were included by consecutive sampling. Using the widespread pain index and severity scale score resulting from hepatitis C infection, patients were evaluated for the existence of fibromyalgia, and information was entered on a predesigned questionnaire. Using SPSS version 24.0, the data that was recorded on the questionnaire was analyzed. The Chi-square test was applied with a significant p-*value *< 0.05.*

Results: *The prevalence of fibromyalgia was reported to be 46.4% (26 individuals), while 53.6% (30 patients) did not have the condition. Fibromyalgia was present in 33.3% of patients below the age of 30 years, 47.1% of patients between the range of 31yrs -50yrs, and 50% of patients above the age of 50 years (p=0.774). In terms of gender, there were 66.7% of female patients with fibromyalgia as opposed to 17.4% of male patients (p=0.001). In terms of WPI, the mean of male respondents was 5.52±5.60, while that of female respondents was 5.52±5.62. (p=0.05) The difference was statistically significant. In contrast, the severity scale score for male respondents was 4.26±3.32 and for female respondents it was 7.12±3.14. The difference was statistically significant (p-value = 0.002).*

Conclusions: *Hepatitis C infection increased the risk of fibromyalgia. Fibromyalgia is highly correlated with gender.*

Keywords: *Fibromyalgia, Hepatitis C Infection, Severity Scale Score (SS), Wide spread Pain Index (WPI)*

INTRODUCTION

A chronic musculoskeletal illness called fibromyalgia syndrome (FS), which is described as widespread tender points and discomfort at certain anatomic locations. Primarily it affects middle-aged women. The prevalence varies depending on the demographic. For adult women, it ranges between 0.7% and 13%, while for adult men, it ranges between 0.2% and 3.9% [1]. A long-standing disorder known as fibromyalgia a new name of old condition, which is described by persistent widespread tender points, exhaustion, disturbed sleep and cognitive impairment[1]. Interstitial cystitis (painful bladder syndrome), headache, temporomandibular joint disorders, irritable bowel syndrome, mastalgia and dysmenorrhea are a few somatic and functional diseases that are frequently linked to biopsychosocial model. Psychological symptoms common in fibromyalgia patients include anxiety and sadness. The majority of patients arrive with a combination of physical, psychological and cognitive symptoms[2]. It is usually related with somatic and functional illnesses for example interstitial cystitis (painful bladder syndrome), headache, temporomandibular joint disorders, irritable bowel syndrome, mastalgia and dysmenorrhea. Anxiety

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and melancholy are two psychological symptoms that fibromyalgia sufferers frequently experience. Most patients enter with a mix of cognitive, psychological and somatic problems[3]. Infection such as Epstein-Barr virus, parvovirus, Borrelia (Lyme disease) and campylobacter infection has been proven to be temporally connected to fibromyalgia among other viral and bacterial infections[4,5]. Patients with hepatitis C or HIV infection had fairly increased rates of fibromyalgia[5,6]. Patients with HCV infection may commonly display rheumatological symptoms such arthralgia, myalgia, arthritis, myositis and fibromyalgia. Other rheumatological symptoms include essential mixed cryoglobulinemia, vasculitis, and sicca symptoms[7,8]. Although, the precise causes of these extra hepatic symptoms of HCV infection and the rheumatological manifestations are yet unknown and it has been hypothesized that immunological processes may be involved. Autoantibodies are frequently seen in the circulation in patients with persistent viral hepatitis. In addition to the deposition of circulating immune complexes in the tissues, viral antigens or viruses can cause local immune complex development that interacts directly with extra hepatic tissues[9]. According to current research, bacterial or viral infections influence the way that pain is processed through neuronal as well as non-neuronal mechanisms by activating certain receptors and releasing pro-inflammatory cytokines[10]. In response to viral and bacterial illness, the peripheral (PNS) as well as central nervous systems (CNS) experience neuroinflammation[10]. Bacterial infection may control primary sensory neurons directly or indirectly by activating receptors on neurons and glial cells.[10] Activation of glial mediators and non-neuronal cells like macrophages or Schwann cells in the PNS. Patients with fibromyalgia have shown signs of both neuro-inflammation and systemic inflammation[11, 12].

For the majority of the 20th century, fibrositis or widespread fibrositis was employed as the diagnostic term[13]. Since the American College of Rheumatology (ACR_1990) categorization criteria were published, fibromyalgia has gained widespread acceptance as a diagnosis and is often utilized by doctors and researchers. It was founded on the opinions of several rheumatologists in the ACR who specialize in fibromyalgia. The primary symptom is widespread chronic tender points that have persisted for more than three months, and the crucial symptoms are 11 of 18 sensitive spots that may be felt while applying pressure of around 4 kg to the axial bone and muscle tendons. The tender point examination is not included in the ACR 2010 diagnostic criteria. Wide Pain Index (WPI) and symptom severity(SS) are used to score patient reports of symptoms(SS). WPI score and the amount of uncomfortable body parts are correlated (total score 0-19). The intensity of the four categories of symptoms—fatigue, restless sleep, cognitive impairment, and somatic symptoms—ranges from no symptom to severe symptoms (0–3). SS scale total scores range from 0 to 12. The Wide Pain Index (WPI 7) and severe symptoms (SS 5) or Wide Pain Index (WPI 3) and (SS 9) criteria define fibromyalgia. Therefore, fibromyalgia and chronic widespread tender points/ pain might be seen as two different chronic syndromes, with fibromyalgia serving as a diagnosis for those who also have concurrent physical and psychological symptoms.

METHODOLOGY

At the Mayo Hospital in Lahore, the hepatitis C patients were enrolled for the diagnosis of fibromyalgia within the designated time period (1st January, 2019 to 30th May 2019, and their age, gender, and known risk factors were taken into account). Hypothyroidism, vitamin D deficiency, steroid intake, hepatitis B, HIV, DM and anemia were excluded by biopsychosocial model (history taking, clinical examination) as well as biochemical testing. The questionnaire data was reviewed and analyzed by using SPSS version 24.0. The frequency data with percentage as well as Means±SD were determined for categorical variables. Chi-square test was performed to examine the relations between various components and socio-demographic data or biopsychosocial model. Wide pain index (WPI) and symptom severity (SS) among gender and duration were calculated using an independent t-test (years). P-values under 0.05 were measured statistically significant.

RESULTS

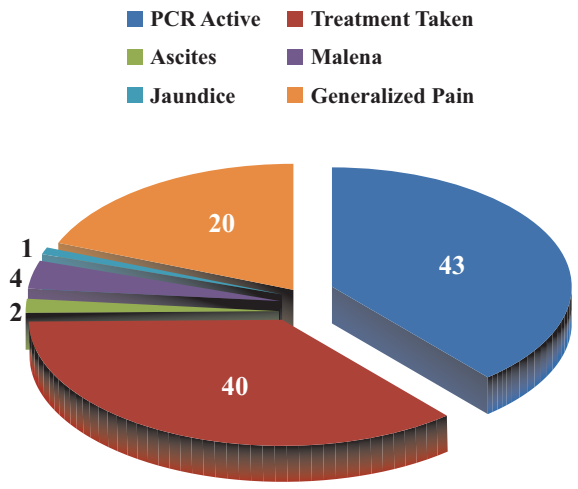
Total 56 patients with hepatitis C presented during the specified time period. Fibromyalgia was reported to be present in 46.4% (26 patients) and 53.6% (30 patients) were not suffering from fibromyalgia. Out of 56 patients presented, 58.9% of patients (33) were males and 41.1% (23) were females, thus making male to female ratio as 1.0:1.435 respectively. The mean WPI was 7.29±5.76 and Severity symptoms showed that 5.95±3.49. Table-I shows the gender and respective age group distribution with mean age as 45.43±11.15 years among the patients with hepatitis C infection. Regarding known factors, there were 10.7% (06) patients having diabetes mellitus (DM), hypertension was seen in 7.1% (04) patients while known symptoms for 3 months were 51.8% (29).

Table I: Frequency distribution of characteristics and certain factors among patients

Variables		Frequency	Percentage
Fibromyalgia	Yes	26	46.4
	No	30	53.6
Age (Years) 45.43±11.15*	≤ 30	06	10.7
	31-50	34	60.7
	> 50	16	28.6
Gender	Males	33	58.9
	Females	23	41.1
Diabetes Mellitus	Yes	06	10.7
	No	50	89.3
Hypertension	Yes	04	7.1
	No	52	92.9
Symptoms for 3 months	Yes	29	51.8
	No	27	48.2
Total		56	100

*Mean ± SD

Figure I: Various factors among Hepatitis C patients.



There were 33.3% patients with fibromyalgia that were having age ≤ 30 years, 47.1% were of ages 31 to 50 years, and 50% were > 50 years (p-value = 0.774). Regarding gender, there were 17.4% male patients with fibromyalgia as compared to 66.7% female patients suffering from the disease (p-value = <0.001) as shown in table no: II.

Table II: Age and Gender association with Fibromyalgia among hepatitis C patients

Variable		Fibromyalgia		p-Value
		Yes (%)	No (%)	
Age (Years)	≤ 30	02 (33.3%)	04 (66.7%)	0.774
	31-50	16 (47.1%)	18 (52.9%)	
	> 50	08 (50%)	08 (50%)	
Gender	Males	04 (17.4%)	19 (82.6%)	<0.001*
	Females	22 (66.7%)	11 (33.3%)	
Total		26 (46.4%)	30 (53.6%)	

* Significant (p-value ≤ 0.05)

The mean shown by male respondents was 5.52±5.60 regarding WPI and among females it was 8.52±5.62. The difference was statistically significant (p-value = 0.05). Whereas severity scale scores showed that male respondents had 4.26±3.32 and female respondents showed mean 7.12±3.14. The difference was statistically significant (p-value = 0.002). Comparing the two scales with disease duration of 3 or more than 3 years show wide spread pain index 7.61±5.42 and 6.61±6.52 respectively. The difference was statistically insignificant (p-value = 0.256). Comparative severity scale score showed mean of 5.58±3.61 and 6.72±3.18. The difference was statistically insignificant (p-value = 0.551) as shown in table no: 3.

Table 3: Wide spread pain index and Severity Scale Score regarding gender and Disease Duration (Years)

Scales	Gender	Mean ± SD	p-value
Wide Spread Pain Index	Males	5.52±5.60	0.05*
	Females	8.52±5.62	
Severity Scale Score	Males	4.26±3.32	0.002*
	Females	7.12±3.14	
Scales	**Disease Duration**	**Mean ± SD**	**p-value**
Wide Spread Pain Index	≤ 3	7.61±5.42	0.256
	> 3	6.61±6.52	
Severity Scale Score	≤ 3	5.58±3.61	0.551
	> 3	6.72±3.18	

* Significant (p-value ≤ 0.05)

DISCUSSION

Hepatitis C virus infection is a rising and significant healthcare problem in Pakistan. The various grades of HCV are observed including the acute and chronic infections leading to liver damage, cirrhosis, and hepatocellular carcinoma. In Hepatitis C patients' fibromyalgia is a problem that requires prompt attention. In our study, individuals with hepatitis C had a 46.4% fibromyalgia prevalence rate. Within HCV clinic groups, the rates of prevalence ranged from 50 to 81 percent for musculoskeletal pain[14,15]. Patients with chronic Hepatitis C Virus frequently experience arthralgias; estimates range from 9 to 23%.

According to all available research, the prevalence of Fibromyalgia in people with Hepatitis C Virus ranges from 10.0 to 18.9%[16]. These prevalence rates are greater than those of Fibromyalgia in cirrhotic patients and healthy individuals. Even though these studies suggest a link between Fibromyalgia and chronic Hepatitis C Virus, at least one recent study questions this relationship. As a result of this study's prospective comparison of the prevalence of HCV infection in Fibromyalgia patients with that of Hepatitis C Virus in the general population, it is possible that chance rather than pathophysiology may be to responsible for the association between Hepatitis C Virus and Fibromyalgia. However, one research stood out as a clear exception. Only 46% of Fibromyalgia FM-positive cases in a tertiary pain clinic reported extensive pain, according to Wolfe et al. This posed numerous significant difficulties[4]. According to their findings, 10.4% of Fibromyalgia patients experienced unilateral pain syndromes, 9.6% only experienced pain in the upper body or in the head and trunk, and 10.4% experienced local pain syndromes that only affected one or two quadrants of the body. The remaining samples displayed further types of "incomplete" distribution patterns[12]. Two pathogenetic explanations for how HCV infection could cause FM have been put out to far. According to the first, viral infection and subsequent HCV-induced inflammation may set off a series of biochemical processes that result in FM development [18]. However, it is unclear, given the information to date, whether FM, an extra hepatic manifestation, is caused by immunological processes or hepatic injury. For instance, several investigations have shown that individuals with severe HCV liver disease had a higher incidence rate of Fibromyalgia[17]. Other research has shown no connection between the symptoms of Fibromyalgia and the degree of liver disease, the source of infection, or the status of therapy[18]. Furthermore, it has been demonstrated that co-diagnosis of Fibromyalgia and Hepatitis C Virus can happen in the absence of consistent changes in liver enzymes[19]. Several studies have informed the percentage of participants meeting the 2011 (or 2010) criteria by the low wide pain index WPI category, including 4.4% of 1411 FM patients in a German clinical research[17], 15.5% of 71 participants in a clinical research conducted in Korea [18]. 2.7% of 80 patients in a Spanish population [20], 17% of 52 cases in a German population study [16], 6-7% of 514 patients in the study of the ACR 2010 criteria [17], 62% in the present report, and 25.9% in a 27-subject Scottish population survey[21]. It should be highlighted that the broad pain estimate used in the German population survey included chest, head, and stomach pain into account.

The prevalence of HCV in Pakistan was estimated to be 12.55% in 2017 by Arshad et al [22]. However, a review conducted by Umar et al from 1992-2208 showed 4.7% prevalence, varying from 0.4% to 33.7% in different regions. It was concluded that Pakistan has higher prevalence than neighboring countries. Also, the variation in prevalence could be due to pocket of infections in various parts of the country [23]. Despite of the significant burden of HCV, we found limited data from Pakistan addressing the Fibromyalgia in HCV cases. Hence, this study may provide the local data that can be compared to international figures. This may help to identify and address the fibromyalgia for better quality of life in HCV cases. Authors suggest further regional studies to address the various aspects of Fibromyalgia.

CONCLUSION

Fibromyalgia occurrence due to hepatitis C infection was higher. Gender was found significantly associated with fibromyalgia. Females had higher percentage suffering from fibromyalgia than males. The wide spread pain index and severity symptom scale score was also significant regarding gender.

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