Research Article

Fibromyalgia syndrome in patients with end stage renal disease on Renal replacement therapy in the Medical City of Baghdad

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ABSTRACT

INTRODUCTION: Fibromyalgia syndrome (FMS) is a chronic non-inflammatory and non-autoimmune musculoskeletal disorder characterized by a chronic widespread musculoskeletal pain and increased tenderness.

OBJECTIVE: To determine the frequency of fibromyalgia syndrome (FMS) in regular haemodialysis and renal transplant patients, and to compare it to the general population.

METHODS: Analytical cross-sectional study recruited 175 Iraqi patients (110 haemodialysis and 65 renal transplant patients), and another 110 healthy individuals as control. Full history and clinical examination by a certified rheumatologist were done. The American College of Rheumatology (ACR) 2010 classification criteria for fibromyalgia syndrome were applied for the case definition. The Beck Depression Inventory and the Cattle Anxiety Inventory were used to assess the depression and anxiety status.

RESULTS: Of the Haemodialysis patients, 10/110(9.1%) had the diagnosis of fibromyalgia syndrome, while 3/65(4.6%) of transplant patients had such a diagnosis. From the control group, 8/110(7.27%) diagnosed. FMS diagnosed more in females, 9/10 in dialysis patients, and all 3 transplant patients with fibromyalgia were females. The features of FMS as fatigue, headache, sleep disturbance, anxiety, and depression were more in end stage renal disease than the control group. Fibromyalgia syndrome was not associated with the duration of dialysis or renal transplant.

CONCLUSION: The frequency of fibromyalgia syndrome in end stage renal disease patients is similar to healthy controls, but fibromyalgia related symptoms are more frequent in haemodialysis and transplant patients.

Key words: Fibromyalgia, Haemodialysis, Renal transplant.

INTRODUCTION

Fibromyalgia syndrome (FMS) is a chronic non-inflammatory and non-autoimmune musculoskeletal disorder characterized primarily by diffuse musculoskeletal pain and sensitivity to mechanical stimulation at soft tissue tender points. It characterized by widespread chronic pain (CWP) with morning stiffness less than one hour, also includes non-musculoskeletal features such as fatigue, anxiety, sleep disturbances, headache, psychological distress, and irritable bowel syndrome (IBS).[1]

In 1990, the American College of Rheumatology (ACR) announced the classification criteria for diagnosing FMS.[2] In 2010, the American College of Rheumatology performed a multicenter study to develop simple, practical criteria for clinical diagnosis of fibromyalgia that do not require a tender point examination. A patient meets the diagnostic criteria for fibromyalgia if the following 3 conditions are met: [3]

1a. The Widespread Pain Index (WPI); a score greater than or equal to 7, and symptoms severity (SS) score is greater than or equal to 5. OR

1b. The WPI score is from 3 to 6 and the SS score is greater than or equal to 9.

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2. Symptoms have been present at a similar level for at least 3 months.
3. The patient does not have a disorder that would otherwise explain the pain.

The prevalence of Fibromyalgia in the general population is between 0.2 and 6.6%, in women between 2.4 and 6.8%, in urban areas between 0.7 and 11.4%, in rural areas between 0.1 and 5.2%, and special populations values between 0.6 and 15%. It is more common at middle age, and there is a strong female preponderance with 9-10:1 female to male ratio.[4,5]

The aetiology of FMS is unknown, but several aspects of its pathogenesis had been investigated. It mostly involves alterations in multiple ascending and descending central nervous system pathways, as well as peripheral pathways, leading to heightened pain sensitivity. Population-based studies have shown that physical and emotional stressors at the workplace and depressed mood are recognized risk factors. A myriad of pathophysiological changes is associated with FMS without any clear causal relationship.[6]

The chronic kidney disease-mineral and bone disorder (CKD-MBD) spectrum include osteomalacia, hyperparathyroid bone disease, adynamic bone disease, and osteoporosis. In addition to the myopathic and neuropathic symptoms that accompany the uraemic syndrome like cramps, weaknesses, restless leg syndrome, and others. Thus, CKD-MBD contribute for these symptoms, but there was no consistent evidence that it has a peculiar mechanistic effect on FMS in haemodialysis (HD) patients. These are not exclusive to HD, renal transplantation also carries important rheumatologic manifestations. FMS limits the physical function of patients and the quality of life of dialysis and renal transplant patients.[7,8]

Two-thirds of patients on regular haemodialysis (HD) have musculoskeletal problems and this increases with time on dialysis. In a study by Haroon et al, FMS was the most common rheumatic manifestation in HD patients with a frequency of 51 %. Sleep disturbances, fatigue, and cognitive symptoms were associated with FMS.[7]

Unpublished report from Iraq about rheumatological manifestations among patients on hemodialysis states that arthralgia and muscle pain are the most common symptoms and tend to increase in frequency with the duration of dialysis.[9]

Literature review revealed contradictory data about the prevalence of FMS in HD patients. In a meta-analysis by Heidari et al, the prevalence of FMS in HD patients was 6.30% compared to the general population 1.78% (95% CI 4.6 -7.9).[10] Samimagham H, et al reported higher prevalence of FMS in Iranian hemodialysis patients.[11] Similar data obtained from Turkey.[12] Yuceturk TE, et al concluded that the prevalence of FMS is similar in HD patients and the general population.[13] This was supported by report from Couto et al.[14] The prevalence of FMS appears to be similar in peritoneal dialysis (PD) patients and control subjects, but the functional disability is common in PD patients with FMS than in patients without FMS.[15]

All these reports agreed that no laboratory test in HD patients correlate with FMS, and its close relation to other somatic features and associated with poor life quality.

This study aims at measuring the prevalence of FMS in Iraqi patients with ESRD on regular haemodialysis or renal transplantation comparing to healthy control group. It also tries to find an association between having FMS and other features.

METHODS

Study Design and Setting: Analytic cross-sectional study was conducted at the Haemodialysis and Rheumatology Units of Baghdad Teaching Hospital and Nephrology and Renal Transplantation Centre, the Medical City of Baghdad during the period from January 2016 to June 2016.

Ethical Approval: All study participants signed a consent form before being recruited in this study which was approved by the research committee of the Medical City.

Case definition: We included 110 participants in haemodialysis group, 65 participants in renal transplant group, and 110 participants in the control group. Haemodialysis group has included patient with end stage renal disease who are on regular haemodialysis maintenance program for > 3 moths. Renal transplant group has included patients who underwent renal transplantation without evidence of graft dysfunction. While the control group has included apparently healthy persons who were visiting the outpatient clinics other than the renal and rheumatology at Baghdad teaching Hospital.

Exclusion criteria: Patients with previous rheumatological disease, trauma and joint complications, history of orthopaedic interventions, and patients with chronic fatigue syndrome following viral diseases, hyperparathyroidism, electrolyte disturbances following chronic renal failure, osteomalacia, diabetes mellitus, acute infections, or limb ischemia after haemodialysis were excluded. These were excluded by reviewing the patient's records and nephrology follow-up notes.

The procedure : All patients interviewed and examined by a certified rheumatologist. They were asked if they had experienced CWP for at least 3 months. The examination included the search for tenderness at 19 points by digital palpation. The ACR criteria applied for diagnosing FMS.

Fatigue was defined as difficulty or inability to initiate activity (subjective sense of weakness); reduced capacity to maintain activity (easy fatigability); or difficulty with concentration, memory, and emotional stability (mental fatigue). Patients may report one or a combination of these symptoms, and they may occur alone or in conjunction with localized complaints.[16]

Anxiety is an emotion characterized by feelings of tension, worried thoughts and physical changes like increased blood pressure. People with anxiety disorders usually have recurring intrusive thoughts or concerns. They may avoid certain situations out of worry. They may also have physical symptoms such as sweating, trembling, dizziness or a rapid heartbeat. The Cattle Anxiety Inventory and The Beck Depression Inventory were used to evaluate anxiety and depression respectively.[17,18]

Irritable Bowel Syndrome (IBS) is a gastrointestinal disorder characterized by chronic abdominal pain and altered bowel habits in the absence of any organic cause. [19]

Outcome: the prevalence of fibromyalgia syndrome (FMS) on regular hemodialysis and renal transplant patients and comparison, to the general population. Prevalence is the proportion of a population who have a specific characteristic in a given time period calculated as the number of people in a sample with characteristic / total number of people in that sample.

Statistical Analysis: IBM Corp. Released in 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp was used for statistical analysis. Discrete variables presented as numbers and percentages. Continuous variables presented as means and standard deviations. Chi-square test used for testing relationships between categorical variables. One-way ANOVA used to determine whether there are any statistically significant differences between the means of two or more independent (unrelated) groups. P-value < 0.05 considered significant.

RESULTS

Table 1 shows the that the mean age of par-

Table 1 | The baseline characteristics of the study groups

	Haemodialysis Group	Renal Transplant Group	Control Group	P Value
Age (Mean±SD) years	38.8 + 14.4	38.6 + 11.2	39.1 + 15.2	0.799
Gender (F/M)	60/50	35/30	58/52	0.964
FMS No. (%)	10 (9.1%)	3 (4.6%)	8 (7.3%)	0.548
Total	110	65	110	

FMS; Fibromyalgia syndrome

Table 2 | The distribution of Renal patients age, gender, and duration of dialysis and transplantation

	FMS Present	FMS Absent	P
Haemodialysis (110)			
Gender F/M	9/1	49/50	0.018
Age			0.034
< 40 years	0	32	
≥ 40 years	10	68	
HD duration			0.236
< 1 year	8	61	
≥ 1 year	2	39	
Renal Transplantation (65)			
Gender F/M	3/0	32/30	0.017
Age			0.04
< 40 years	0	42	
≥ 40 years	3	20	
Transplant duration			0.161
< 1 year	3	37	
≥1 year	0	25	

FMS: Fibromyalgia syndrome, HD: Haemodialysis, F/M: Female to male

ticipants was 38+14.4, 38+11.2, and 39.1+15.2 years in haemodialysis, renal transplant, and control groups respectively. In all groups, females are slightly predominant than males. FMS was present in 10 patients (9.1%) in haemodialysis group, in 3 patients (4.6%) in renal transplant group, and in 8 (7.3%) participants in the control group; however, this difference was statistically non significant, p value is 0.548.

Table 2 shows the effect of gender, age below 40 years or above, and duration of being on haemodialysis or renal transplant less than or more that a year on presence or absence of FMS. The difference for age and gender were statistically significant although the numbers in some subgroups are very small.

Table 3 shows the presence or not of the number of tender points, sleep disturbances, fatigue, numbness, anxiety, depression, IBS, and headache among the three groups. All show a statistical significance except for the number of tender points.

DISCUSSION

The current study shows that the frequency of FMS in HD and transplant recipients is not different from the healthy controls (p-value =0.54). This will add to the heterogeneity of evidence regarding the true prevalence of FMS in renal patients when compared to the general population. Racial and regional variations may explain such heterogenous data.[13] Prospective multicenter study with a larger sample may answer this question for a specific country or geographical region like the Middle East.

FMS is more common in women in both renal patients and the general population and this is consistent with other data. Wolfe and co-workers revealed in a random sample of 3006 adults that the prevalence of FMS is 3.4% in women and 0.5% in men.[20]

This study shows a significant relation of FMS with age. All renal patients with FMS were 40 years and older. This is consistent with the general notion that it often occurs in older persons.[20]

Similar to the previous studies, there was no link between the duration of dialysis and the frequency of fibromyalgia as well as the time since renal transplantation.[14] Samimagham H et al and Leblebici B et al reported higher prevalence of FMS in HD patients than the general population. The range of dialysis duration in these studies were (3-312) and (6–210) months respectively. Thus, FMS was not related to longer dialysis duration.[12,13]

The features that frequently accompany FMS include fatigue, sleep disturbances, anxiety, depression, and headache. This study reveals that the frequencies of such features were higher in HD and transplant patients than control subjects. In both fibromyalgia and ESRD, a central nervous system dysfunction, and metabolic derangements associated with sleep and mood disorders. Thus, fibromyalgia patients are often at increased risk for depression.[11] Depression is a common finding in Iraqi HD patients.[21] There was a significant difference in the levels of the anxiety between the patients and control groups, especially in HD patients.[15]

The pathogenesis of FMS and IBS remain unclear, but it is likely related to dysregulation

Table 3 | Comparison between the study groups according to tender points and associated symptoms

Variables	Haemodialysis (110)		Renal transplant (65)		Control (110)		P
	N	%	N	%	N	%	
Tender Points							
>11	11	10	3	4.6	8	7.3	0.524
<11	99	90	62	95.4	102	92.7	
Sleep Disturbances							
Yes	43	39.1	31	47.7	22	20	0.000
No	67	60.9	34	52.3	88	80	
Fatigue							
Yes	37	33.6	37	56.9	25	22.7	0.000
No	73	66.4	28	43.1	85	77.3	
Numbness							
Yes	14	12.7	13	20	5	4.5	0.006
No	96	87.3	52	80	105	95.6	
Anxiety							
Yes	42	38.2	32	49.2	8	7.3	0.000
No	68	61.8	33	50.8	102	92.7	
Depression							
Yes	43	39.1	28	43.1	6	5.5	0.000
No	67	60.9	37	56.9	104	94.5	
IBS							
Yes	42	38.2	34	52.3	26	23.6	0.001
No	68	61.8	31	47.7	84	76.4	
Headache							
Yes	44	40	22	33.8	18	16.4	0.000
No	66	60	43	66.2	92	83.6	

IBS; Irritable bowel syndrome

within the brain-gut axis, resulting in a hyperalgesic state. IBS and FMS share other similarities, including a female predominance, fatigue, insomnia, and susceptibility to psychiatric state. These common manifestations and pathogeneses serve as a foundation for overlapping, multidisciplinary treatment modalities.[22]

FMS and these associated somatic features will affect patient's quality of life. Hemodialysis itself has a negative impact on the quality of life (QOL) of Iraqi patients and worldwide.[23] Patients who underwent kidney transplantation have a significantly better quality of life than those who continue on maintenance hemodialysis.[24] Despite, this improvement on transplantation, FMS still tends to occur in transplant recipients. This may be related to altered psychology or it may be attributed to immunosuppression and other factors. Immunosuppressive medications provoke more metabolic and neurological issues in renal transplant patients which in turn may contribute to FMS. It is reported that in renal transplant recipients, FMS was strongly associated with hypertension, arterial stiffness, obesity, and renal allograft dysfunction.[25]

This study was limited by being only a single-center study. It didn't study the effect of dialysis adequacy on the frequency of FMS, and the effect of immunosuppression has not been emphasized.

CONCLUSION

In conclusion, the frequency of FMS in ESRD patients is similar to healthy controls, but FMS related symptoms are more frequent

in haemodialysis and transplant patients. Larger multicenter study needed to have the exact prevalence of fibromyalgia in Iraqi haemodialysis and renal transplant patients.

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Abbreviations list: American College of Rheumatology (**ACR**), Analysis of variance (**ANOVA**), End stage renal disease (**ESRD**), Fibromyalgia syndrome (**FMS**), Haemodialysis (HD), Irritable bowel syndrome (**IBS**), Peritoneal dialysis (**PD**), Quality of life (**QOL**), Statistical Package for the social science (**SPSS**), The chronic kidney disease-mineral and bone disorder (**CKD-MBD**), widespread chronic pain (**CWP**).

Conflict of interest: Authors have nothing to disclose.

Funding: Nothing apart from self-funding.

The editorial board of the ***Iraqi NMJ*** expresses its deep condolences for the death of the principal author of this article, **Dr Khudir Z. Al-Badri** who passed away struggling of COVID-19 while we were pursuing the review of his article.