IMPACT OF FIBROMYALGIA ON DAS-28 SCORE IN RHEUMATOID ARTHRITIS

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ABSTRACT

Objective: To determine the frequency of fibromyalgia American college of rheumatology (ACR) 2010/2011 criteria) in patients with rheumatoid arthritis and its impact on disease activity score (DAS-28).

Study Design: Cross-sectional study.

Place and Duration of study: Department of Rheumatology and Immunology, Sheikh Zayed Hospital Lahore from Jun 2016 to Feb 2017.

Patients and Methods: Total 140 diagnosed patients of rheumatoid arthritis by criteria ACR 2010 were included in this study. ACR modified 2010/2011 criterion of fibromyalgia was used to diagnose co existing fibromyalgia in these patients. Clinically disease activity status was assessed by standardized and validated DAS-28 calculator; 2ml of blood was drawn and sent to laboratory for estimation of erythrocyte sedimentation rate for all study participants.

Results: The mean age, duration of disease, DAS-28 of sampled population was 49.12 ± 8.5 years, 7.36 ± 3.8 years, 4.08 ± 1.1 respectively. Out of 140 patients, 127 patients (90.7%) were females. Fibromyalgia was diagnosed in 41 patients (29.1%). The mean DAS-28 score in patients of rheumatoid arthritis with fibromyalgia was 5.39 ± .58 while for patients of without fibromyalgia it was 3.54 ± 0.69 (p-value<0.001).

Conclusion: Secondary fibromyalgia is common in patients with rheumatoid arthritis and needs to be screened out in all patients diagnosed as rheumatoid arthritis and on subsequent follow up visits, coexisting fibromyalgia affects the disease activity status and this may result into inappropriate and unnecessary changes in treatment plans.

Keywords: Fibromyalgia, Impact, Rheumatoid arthritis.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic systemic autoimmune disorder, which not only involves the joints symmetrically but also involves the other organs of body[1,2]. The RA may clinically remit with the use of medicines called disease modifying anti rheumatoid drugs[3-5]. These drugs not only improve the symptoms and signs of active RA, but also halts the ongoing structural joint damage and stop functional impairment[6]. In developing countries like Pakistan, we rely on conventional non-biological agents for treatment[7,8]. Fibromyalgia is commonly coexisting diagnosis in patients with rheumatoid arthritis and other autoimmune diseases. FM is a clinical syndrome in which central pain processing is defective leading to widespread musculoskeletal pain and fatigue along with physical and psychological impairment[9-12]. Various studies have shown the prevalence of fibromyalgia about 12-17% among patients with rheumatoid arthritis[1,7,13]. Its prevalence varies with population and gender of the patients it was noted that female gender was more associated with rheumatoid arthritis and fibro-myalgia (RAFM) phenomenon[7,8,14]. Disease activity score (DAS) calculation is the cost effective, easy and most extensively used method to assess the current clinical disease status in RA patients. On the basis of the DAS-28 score clinicians decide to escalate or deescalate the conventional synthetic DMARD's doses or try to introduce biological DMARD's. A modified version in practice for disease activity assessment is DAS-28, which provides a global summative and continuous score[7,9,12]. In a developing country like Pakistan, where cost of the treatment is the major factor in determining the compliance of the patients, co-

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existing fibromyalgia in RA patients may lead to over assessment of disease activity, which may lead to inappropriate escalation in the disease therapy. Previously fibromyalgia was diagnosed using 19 tender point examination[15]. Now there is a change in guidelines for diagnosis. There is only one local study available describing the prevalence of fibromyalgia among rheumatoid arthritis patients with 1990 diagnostic criterion[7]. Similarly only one local study is available showing relation between DAS-28 in patients of rheumatoid arthritis with and without co-existing fibromyalgia but they had used 1990 ACR criteria for diagnosis of FM[8]. Rationale of study is to know the prevalence of fibromyalgia in Pakistani patients with rheumatoid arthritis by using modified 2010 ACR criteria for diagnosis of FM and its impact on DAS-28 score.

MATERIAL AND METHODS

After the approval of ethical review committee, this cross-sectional study was undertaken in out patient department of Rheumatology & Immunology, Sheikh Zayed Hospital Lahore from 1st June 2016 to 28th February 2017. Using non-probability consecutive sampling, all patients diagnosed as seropositive rheumatoid arthritis on the basis of ACR 2010/2011 criteria[6] were asked to participate in study. History with other autoimmune disorder (SLE, systemic sclerosis, polymyositis), osteoarthritis, hypothyroidism, chronic fatigue syndrome, depression, patients taking antipsychotic medicines, malignancy, history of chemotherapy or radiotherapy in last 5 years, patients undergoing dialysis, chronic liver disease, congestive cardiac failure, alcoholics and those diagnosed as diabetes mellitus were excluded. The sample size of 140 was calculated by taking prevalence of fibromyalgia (22%) with 7% margin of error and 95% confidence level. All those fulfilling the inclusion criteria of study, verbal and written consent were obtained. Data were collected on specifically designed data questionnaire containing background information like age in years, gender, time since diagnosis of RA, clinical parameters related to diagnosis of fibromyalgia (2010/2011 ACR criteria) and DAS-28[6]. Fibromyalgia was diagnosed on the basis of modified ACR 2010 criteria consisting of widespread pain inventory (WPI) and symptom severity scale[15]. Blood sample was drawn by trained phlebotomist and taken immediately to Sheikh Zayed pathology laboratory, for analysis of ESR. DAS-28 score was calculated using standard calculator which includes total number of swollen joints, total number of tender joints, patient's global assessment and ESR. Data were analyzed on computer using SPSS version 20.0 software program. Mean and standard deviation was calculated for age, time since diagnosis of RA and DAS-28 score. While frequencies and percentages were mentioned for sex and fibromyalgia. The mean difference in DAS-28 scores in patients of rheumatoid arthritis (RA) with and without co existing fibromyalgia was analyzed using inde-pendent samples t-test. While presence of fibro-myalgia was stratified for age, gender. Post stratification Chi square and Fischer exact test were applied. A *p*-value of <0.05 was considered as significant.

RESULTS

In our study, the mean age was 49 years. Most of study participant were females (90.7%) with mean disease duration of seven years. Among sampled population, 29.3% patients had co existing fibromyalgia. Mean disease activity score in the sampled population was 4.08 ± 1.1. All baseline characteristics are presented in table-I. Baseline parameters were statistically similar between patients of RA with and without fibromyalgia except disease activity score which was statistically high among patients of RA with fibromyalgia. Detailed differences are presented in table-II.

DISCUSSION

Rheumatoid arthritis with fibromyalgia (RAFM) is the phenomenon, which adversely affects commonly used disease activity score like DAS-28[1,10,12,13,16]. DAS-28 is important in measuring the disease activity so to modify treatment of RA, especially decision regarding the use of medicine which may alter the course of

disease. As there were changes in diagnostic criterion of fibromyalgia, we were expecting a difference in prevalence and effect on DAS-28[9]. Therefore, this study was conducted in RA patients to determine the impact on DAS-28 score with co-existing fibromyalgia with latest fibromyalgia (FM) ACR 2010 criteria. In our study, prevalence of fibromyalgia based on modified diagnostic criteria was 29.3%. This result shows high prevalence as compared to previous studies. In the previous Pakistani study in diagnosed cases of RA[7]. Our study results are in line with previous studies showing similar age, gender and duration of disease distribution even in multi ethnic populations[1,10-13,16]. To determine the impact of fibromyalgia's presence or absence on DAS-28, we compared scores in both groups. The mean DAS-28 score in sampled population was 4.08 ± 1.1. It implies ongoing moderate disease activity in general. This is also worse as reported by international studies[9,16]. The difference may be due to prevalent use of biological

Table-I: Descriptive statistics and fibromyalgia of sampled population of rheumatoid arthritis patients (n=140).

Characteristics		Frequency	Percentage (%)
Gender n(%)	Male	13	9.3
	Female	127	90.7
Fibromyalgia	Yes	41	29.3
	No	99	70.7
Age (years)	Mean ± SD	49.12 ± 8.5	
Disease duration (years)	Mean ± SD	7.36 ± 3.8	
DAS-28 score	Mean ± SD	4.08 ± 1.1	

Table-II: Effect of baseline statistics on fibromyalgia in sampled population of rheumatoid arthritis patients (n=140).

Characteristics		Fibromyalgia N=41	No Fibromyalgia N=99	*p*-value
Gender	**Male**	5 (12.2%)	8 (8%)	0.52*
	Female	36 (87.8%)	91 (91%)	
Age in years	Mean ± SD	49.4 ± 9.1	49 ± 8.3	0.795*
Disease duration	Mean ± SD	7.2 ± 3.9	7.4 ± 3.8	0.753**
Disease activity score (DAS-28)	Mean ± SD	5.39 ± .58	3.54 ± 0.69	<0.001***

*Statistically non-significant, **Statistically non-significant while assuming non-equal variance, ***Highly significant.

by Zammurrad *et al*, RAFM was reported as 22.4%[8]. The difference may be either due to sampling technique or newer diagnostic criterion. As reported by Gist *et al* out of 117 RA patients, 33.3% (n=39) met 1990 ACR FM criteria and 41.9% (n=49) met 2010 ACR FM criteria[9]. This shows that latest diagnostic criterion for fibromyalgia is more sensitive as compared to previous one. Ranzolin *et al.* in their study showed the prevalence of FM among RA was 13.4%[16] Dhir *et al.* reported 15% fibromyalgia in RA, compared to 2.5% of controls[11]. Abbasi *et al.* presented that 25.83% patients had fibromyalgia anti rheumatic drugs in developed countries, which are not affordable in our setting. While the mean score in patients of RA diagnosed with fibromyalgia was 5.39 ± 0.58 on DAS-28 calculator and for patients without fibromyalgia it was 3.54 ± 0.69. This difference was statistically significant. The other known confounders/effect modifiers like age and disease duration were same in both groups. These results are in accordance with the previously reported results. Study by Ranzolin *et al.* DAS-28 score was higher in RA with coexisting FM (5.36 ± 0.99) than RA without fibromyalgia (FM) (4.03 ± 1.39; $p<0.001$)[16].

Only Gist *et al*. has reported comparable RA disease activity (DAS-28: 3.09 vs. 3.27, *p*=NS) in both groups i.e. RA patients with and without fibromyalgia[9]. Study conducted by Abbasi *et al.* reported median (IQR) DAS-28 score in RA group was 4.9 (3.66-5.71), while in RAFM 7.04 (6.62-7.64)[7]. Vilasica *et al*. in their study also noted that coexisting fibromyalgia increases the DAS-28 scores especially in females[17]. Leeb *et al* also in study proposed that fibromyalgia should be taken into account while calculating the DAS-28 score as co-existing fibromyalgia leads to over-estimation[18]. Niranjo *et al* noted that patients with coexisting fibromyalgia were having a worse functional capacity and poorer quality of life as compared to those RA patients without fibro-myalgia[19]. Dolan *et al* in their review article describes that FM is highly prevalent in patients with RA; studies report that up to 1 in 5 patients with RA fullfill the criteria of fibromyalgia in the disease course[20]. The pathophysiology of secondary fibromyalgia is dependent on multiple factors like cultural, psychosocial, and nutritional factors like low levels of vitamin D[21,22]. Hollick FM has suggested that while dealing with patients of RAFM one should look for the levels of vitamin D and if found low then it must be corrected[21]. This study has few limitations like single center study, small size sample, non-probability sampling and didn't include the confounders of disease activity in rheumatoid arthritis e.g. Vitamin D levels,while strong point is this is first of its kind of study which included the modified ACR 2010 criteria for fibromyalgia while all previous studies had used 1990 criteria which has lower detections rate of FM.

CONCLUSION

It is concluded that the secondary fibromyalgia in patients of RA is quite high and should be considered for screening with initial diagnosis and each subsequent visit during follow up period. It has implication over the routinely used disease activity monitoring score as RA with fibromyalgia participants had high DAS-28 score in comparison to other group without fibromyalgia, so frequent changes in treatment must be carefully made once such factors are ruled out.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

REFERENCES

1. Joharatnam N, McWilliams DF, Wilson D, Wheeler M, Pande I, Walsh DA. A cross-sectional study of pain sensitivity, disease-activity assessment, mental health, and fibromyalgia status in rheumatoid arthritis. Arthritis Res Ther 2015; 17: 11.
2. Shamim R, Jan MD, Zafar U. Prevalence of rheumatoid arthritis in population with arthralgia presenting to a tertiary care hospital. J Pak Med Assoc 2015; 65(11): 1202-5.
3. Khalil Z, Salim B, Nasim A, Malik S. Patients' knowledge on Rheumatoid Arthritis - A study at a tertiary care hospital. J Pak Med Assoc 2017; 67(2): 256-60.
4. Makhdoom A, Rahopoto MQ, Awan S, Tahir SM, Memon S, Siddiqui KA. Bone mineral density level by dual energy X-ray absorptiometry in rheumatoid arthritis. J Pak Med Assoc 2017; 67(1): 15-9.
5. Jalil SF, Arshad M, Bhatti A, Ahmad J, Akbar F, Ali S, et al. Rheumatoid arthritis: What have we learned about the causing factors? Pak J Pharm Sci 2016; 29(2): 629-45.
6. Saag KG, Teng GG, Patkar NM, Anuntiyo J, Finney C, Curtis JR, et al. American College of Rheumatology 2008 recommendations for the use of nonbiologic and biologic disease modifying antirheumatic drugs in rheumatoid arthritis. Arthritis Care & Research 2008; 59(6): 762-84.
7. Abbasi L, Haidri FR. Fibromyalgia complicating disease management in rheumatoid arthritis. J Coll Physicians Surg Pak 2014; 24(6): 424-7.
8. Zammurrad S, Munir W, Farooqi A. Disease activity score in rheumatoid arthritis with or without secondary fibromyalgia. J Coll Physicians Surg Pak 2013; 23(6): 413-7.
9. Gist AC, Guymer EK, Eades LE, Leech M, Littlejohn GO. Fibromyalgia remains a significant burden in rheumatoid arthritis patients in Australia. Int J Rheum Dis 2017.
10. da Silva Chakr RM, Brenol JC, Behar M, Mendonca JA, Kohem CL, Monticielo OA, et al. Is ultrasound a better target than clinical disease activity scores in rheumatoid arthritis with fibromyalgia? A case-control study. PLoS One 2015; 10(3): e0118620.
11. Dhir V, Lawrence A, Aggarwal A, Misra R. Fibromyalgia is common and adversely affects pain and fatigue perception in North Indian patients with rheumatoid arthritis. J Rheumatol 2009; 36(11): 2443-8.
12. Coury F, Rossat A, Tebib A, Letroublon MC, Gagnard A, Fantino B, et al. Rheumatoid arthritis and fibromyalgia: a frequent unrelated association complicating disease management. J Rheumatol. 2009; 36(1): 58-62.
13. Inanc N, Yilmaz-Oner S, Can M, Sokka T, Direskeneli H. The role of depression, anxiety, fatigue, and fibromyalgia on the evaluation of the remission status in patients with rheumatoid arthritis. J Rheumatol 2014; 41(9): 1755-60.
14. Imran MY, Saira Khan EA, Ahmad NM, Farman Raja S, Saeed MA, Ijaz Haider I. Depression in Rheumatoid Arthritis and its relation to disease activity. Pak J Med Sci 2015; 31(2): 393-7.
15. Wolfe F, Clauw DJ, Fitzcharles MA, Goldenberg DL, Katz RS, Mease P, et al. The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and

measurement of symptom severity. Arthritis care & research 2010; 62(5): 600-10.
16. Ranzolin A, Brenol JC, Bredemeier M, Guarienti J, Rizzatti M, Feldman D, et al. Association of concomitant fibromyalgia with worse disease activity score in 28 joints, health assessment questionnaire, and short form 36 scores in patients with rheumatoid arthritis. Arthritis Rheum 2009; 61(6): 794-800.
17. Roig Vilaseca D, Hoces Otero C. [Effect of the Coexistence of Fibromyalgia in the DAS28 Index in Women With Rheumatoid Arthritis]. Reumatol Clin 2008; 4(3): 96-9.
18. Leeb BF, Andel I, Sautner J, Nothnagl T, Rintelen B. The DAS 28 in rheumatoid arthritis and fibromyalgia patients. Rheumatology (Oxford) 2004; 43(12): 1504-7.
19. Naranjo A, Ojeda S, Francisco F, Erausquin C, Rua-Figueroa I, Rodriguez-Lozano C. Fibromyalgia in patients with rheumatoid arthritis is associated with higher scores of disability. Annals of the rheumatic diseases 2002; 61(7): 660-1.
20. Dolan L, Tung L, Raizada S. Fibromyalgia in the Context of Rheumatoid Arthritis: A Review. Fibrom Open Access 2016; 1(103): 2.
21. Holick MF. The vitamin D epidemic and its health consequences. J Nutrit 2005; 135(11): 2739S-48S.
22. Bhatty SA, Shaikh NA, Irfan M, Kashif SM. Vitamin D deficiency in fibromyalgia. J Pak Med Assoc 2010; 60(11): 949-51.