PREVALENCE OF RHEUMATOID ARTHRITIS AND ITS PHARMACOLOGICAL TREATMENT IN TWIN CITIES OF PAKISTAN

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Abstract

Rheumatoid arthritis (RA) is a common autoimmune inflammatory arthritis in adults. The present study was conducted to find the prevalence of RA in different genders, age groups and treatment regimen prescribed to patients for 6 months. Convenience sampling method was used in collecting data of RA patients via questionnaire. Results showed that RA is higher in females (72.61%) than men (27.39%). A sharp increase in RA prevalence was notice in patients with above 60 years old. Mostly patients suffering from this disease were unemployed and had limited physical activity, thus higher BMI (overweight, obese and extra obese) was observed within these patients. Many of the patients had been diagnosed with Rheumatoid Factor (RF) Test, and Lacosamide drugs, as pain reducer, was prescribed by doctors the most to the RA patients. Statistically, there was non-significant (P value>0.05) association between demographic data of the RA patients and diagnostic tests (RF test and anti-cyclic citrullinated peptide (ACCP) antibodies) as well as drugs prescription. This study clearly showed that a prime factor involving in RA that help the community to prevent this disease is by improving the quality of life such as proper diet along with mild exercise or physical activity in order to prevent this autoimmune disease.

Keywords: Rheumatoid arthritis, BMI, anti-cyclic citrullinated peptide (ACCP) antibodies, rheumatoid factor (RF), lacosamide.

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INTRODUCTION

Rheumatoid arthritis (RA) is a chronic progressive inflammatory disease of unknown etiology characterized by polyarticular symmetric joint involvement and systemic manifestations (1). RA commonly affects joints in the hands, wrists, and knees. In a joint with RA, the lining of the joint becomes inflamed, causing damage to the joint tissue (2). This tissue damage can cause long-term or chronic pain, instability (lack of balance), and deformity (disfigurement). The epidemiology of RA shows a population prevalence of 0.5% to 1% and a highly variable annual incidence (12-1200 per 100,000 populations) depending on sex, race/ethnicity, and calendar year. People with RA have a significantly shortened life expectancy compared to non-RA controls (3).

The difference in the incidence and prevalence of RA between the genders suggests that there are more factors associated with the female gender that play a role in the development and progression of RA. However, studies on hormonal differences have produced conflicting results. For example, pregnancy and breastfeeding have been associated with a reduced risk of developing RA. At the same time, postpartum and postmenopausal periods and especially early menopause (up to 44 years) were associated with an increased risk (4). Causes of death are not significantly different between patients with RA and the general population from which they are drawn. It can be said that most affected individuals die from the same causes as the general population, but at a younger age (5).

Several potential genetic factors are associated with the increased incidence of RA, including the occurrence of the so-called common epitope in HLA class II molecules, gene polymorphisms of some matrix metalloproteinases (MMP), including matrix metalloproteinase 1 (MMP-1) and matrix metalloproteinase 3 (MMP-3), as well as polymorphism of pro-inflammatory cytokine genes, especially tumor necrosis factor α (TNF-α), interleukin 1β (IL-1β) and interleukin 4 (IL-4). In addition to genetic factors, environmental factors play a special role etiopathogenesis of RA, including smoking, long-term stress, improper diet and Intensive exercise (6). An important concept that has emerged in the understanding of risk factors for RA is the role of anti-citrullinated protein/peptide antibodies (ACPA), also known as anti-cyclic citrullinated peptide (ACCP) antibodies. ACPA is a more specific marker for RA than rheumatoid factor and is believed to be involved in the pathogenesis of the disease (7).

The average age of onset of RA in Pakistan is 37 years, also significant proportion of RA cases still remain undiagnosed in our community (8). Thus, the present research objectives were to study the effectiveness of treatment used for RA patients in different health care system of twin cities (Islamabad and Rawalpindi) of Pakistan, as well as to assess the risk ratio of RA.

METHODOLOGY

This descriptive observational study was conducted in taking response of RA outpatients of PIMS, Islamabad and PEMH Rawalpindi. Convenience sampling method was used, and the estimate sample size of patients was collected from total 157 patients. The demographic information gathered from the patient included gender, age, area, marital status, weight, menopause, occupation and living conditions. The patient data other than demographic information included history of present illness (HOPI), past medical history (PMH) and family history (FH). Parameters that was observed of the patients were dose of drugs, duration of therapy, diagnosis of RA, cost of therapy, strength of drug prescribed, prevalence in males and females, and number of other drugs prescribed.

Inclusion and exclusion criteria

Patients of all ages, both gender: male and female, and patient with co morbidities were included for data collection, however, pregnant females and patient who had undergone recent orthopedic surgery were excluded from study.

Statistical analysis

Data collected was analyzed using SPSS ver20. The frequency and percentage was determine of all parameter, and association among demographic characteristics and lab test as well as drugs usage was determine with 95% confidence level and significant being P value<0.05.

RESULTS

The demographic information of the present study total participants, which were 157, showed that female were in higher number (72.61%) than of male (27.39%)(table 1). As regard to age, the highest number of participants were within age group 55-74 years old (48.41%), followed by participants within aged group of 75-94 years (28.66%). The least number of participants were observed for participants with aged group 35-54 (10.19%). Overall, participants above 60 were much higher than those participants below 60 years old. According to the BMI of the RA patients, only 5.73% had normal BMI, whereas all other were

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overweight (22.93%), obese (20.38%) and extra obese (50.96%).

Table 1: Demographic characteristics of RA patients

Demographic data		Frequency	(%)
Gender	Female	114	(72.61%)
	Male	43	(27.39%)
Age	15-34	20	(12.74%)
	35-54	16	(10.19%)
	55-74	76	(48.41%)
	75-94	45	(28.66%)
BMI	Under weight	0	0.00
	Normal	9	(5.73%)
	Over weight	36	(22.93%)
	Obese	32	(20.38%)
	Extra obese	80	(50.96%)
	Total	157	(100%)

The presence of RA according to laboratory test showed that there were many patients that used RF test (57.32%) and less patients for RA did ACCP Ab (42.68%). Further, results showed that female used the RF test, whereas male had been observed using mostly ACCP test for RA. Among the age groups, those patients that were below 35 years old used mostly ACCP test, and above 35, many preferred using RF test for RA. As for BMI, highest RF test was preferred compared to ACCP Ab in all BMI groups including normal, overweight, obese and extra obese. Statistically, there was no significant (P value>0.05) association between laboratory test and demographic characteristics (gender, age and BMI).

Table 2: Cross tabulation of demographic characteristics and lab tests of RA patients.

Demographic data		ACCP Ab		RF test		P value
		Frequency	(%)	Frequency	(%)	
Gender	Female	44	(28.03%)	70	(44.59%)	0.09
	Male	23	(14.65%)	20	(12.74%)	
Age	15-34	12	(7.64%)	8	(5.10%)	0.15
	35-54	4	(2.55%)	12	(7.64%)	
	55-74	30	(19.11%)	46	(29.30%)	
	75-94	21	(13.38%)	24	(15.29%)	
BMI	Underweight		0.00		0.00	
	Normal	4	(2.55%)	5	(3.18%)	0.702
	Overweight	17	(10.83%)	19	(12.10%)	
	Obese	11	(7.01%)	21	(13.38%)	
	Extra Obese	35	(22.29%)	45	(28.66%)	
	Total	67	(42.68%)	90	(57.32%)	

Present results showed that both gender, male and female, the highest prescribed drugs for RA treatment was lacosamide, followed by leflunomide (22.93%) in females and hydrochloroquine prescribed by male mostly for RA treatment. The least drugs that was prescribed for RA patients was methotrexate for both male (3.82%) and female (8.92%). Lacosamide and leflunomide were considered as the most prescribed drugs because RA patients of every age group had shown that mostly these drugs are used by patients for RA treatment. The least usage of drugs among the research study patients seemed methotrexate followed by hydrochloroquine. Similarly, no difference was observed as such for patients of different BMI. Statistically there was no significant (P value>0.05) association between drugs used by RA patients demographic characteristics (gender, age and BMI).

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Table 3: Cross tabulation of demographic characteristics and drugs usage in RA patient

Demographic data		Hydrochloroquine Frequency (%)		Lacosamide Frequency (%)		Leflunomide Frequency (%)		Methotrexate Frequency (%)		P value
Gender	Female	22	(14.01%)	42	(26.75%)	36	(22.93%)	14	(8.92%)	0.30
	Male	13	(8.28%)	16	(10.19%)	8	(5.10%)	6	(3.82%)	
Age	15-34	4	(2.55%)	9	(5.73%)	6	(3.82%)	1	(0.64%)	
	35-54	5	(3.18%)	5	(3.18%)	4	(2.55%)	2	(1.27%)	
	55-74	17	(10.83%)	31	(19.75%)	21	(13.38%)	7	(4.46%)	0.44
	75-94	9	(5.73%)	13	(8.28%)	13	(8.28%)	10	(6.37%)	
BMI	Under weight		0.00		0.00		0.00		0.00	
	Normal	1	(0.64%)	3	(1.91%)	3	(1.91%)	2	(1.27%)	
	Over weight	4	(2.55%)	13	(8.28%)	13	(8.28%)	6	(3.82%)	0.34
	Obese	12	(7.64%)	9	(5.73%)	7	(4.46%)	4	(2.55%)	
	Extra obese	18	(11.46%)	33	(21.02%)	21	(13.38%)	8	(5.10%)	
	Total	35	(22.29%)	58	(36.94%)	44	(28.03%)	20	(12.74%)	

The correlation between each of the variables showed that BMI with age had shown a significant (P value<0.05) association with age, however; all the other variables showed no significant (P value>0.05) association with each other (Table 4).

Table 4: Association between all the research variables

Variables	1.	2.	3.	4.	5.
1. Gender	--				
2. Age	-0.119	--			
3. BMI	-0.013	-0.167*	--		
4. Lab test	0.134	-0.005	0.016	--	
5. Drugs	-0.059	0.106	-0.026	-.0.133	--

Note: Correlation is significant at the 0.05 level.

Discussion

The global prevalence of RA between 1980 and 2019 was 460 per 100,000 population, with variations due to geographical location and study methodology (9).The prevalence of rheumatoid arthritis (RA) in different regions have been significant increases in North Africa and the Middle East (13% since 1990) and Western Sub-Saharan Africa (14%), while rates have decreased in Eastern, Central, and Southern Sub-Saharan Africa (4-12%). The challenges of low disease awareness, delayed visits to rheumatologists, and socioeconomic factors hinder early diagnosis and effective treatment. In many countries other factors are lacking like limited access to treatments for both physicians and patients due to the lack of RA-specific treatment guidelines and resources (10).

The present study showed that RA prevalence was higher in females, mostly above 60 years old and which had higher BMI i.e. overweight, obese or extra obese. The data also showed that there was sharp increase of RA in patients above 55 years old. These results were supported by Sparks et al. (11), who stated that RA risk had increased in patient that were above 55 years old. Elderly RA patients are growing because of increase in longer life spans. Late-onset RA has shown distinct clinical and possibly biological differences from early-onset RA. On the other hand, managing RA in older patients is complex, requiring a balance between effective treatment strategies and potential complications due to age-related health issues. Therefore, preference for RA patients is to have less aggressive treatment approaches (12). Targonska-Stepniak et al. (13) findings, which founded that there were higher number of male that were diagnosed with RA compared to females, showed conflict with the present study regarding gender findings i.e. females patients were higher

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than male RA patients. However, in another study conducted by Khaliq et al. (14) showed that in Islamabad the prevalence of RA was higher in females (71.4%) compared to males (28.6%).

Diagnosis of RA in present study patients was proceeded by ACCP ab and RF test, where most of the patients used RF test, and less were diagnosed via ACCP Ab. Within groups, it was found that female patients had used mostly RF test whereas in male, ACCP Ab was used for RA diagnosis. Further, no significant association was seen between the laboratory tests and demographic characteristics (gender, age and BMI). Al-Kefaee et al. (15) conducted similar study, in which females' frequency of RA disease was greater than male, with female to male ratio being 5.6:1. Further ACCP antibodies test was more specific to be used compared to the RF test for diagnosing/predicting of RA. In a study conducted by Ahmed and Al-Sadoon (16) found that in Iraq, patients with RA had significant association with BMI. Our study had non-significant association of the tests and BMI, which might be because of small sample numbers as well as there were no control group that could be used for RA patients.

As for drugs that were used in treatment of RA patients, Lacosamide was found to be prescribed to patients, followed by leflunomide, hydrochloroquine and the least prescription was noticed for Metotrex. Also there was no significant association observed between the drug used and demographic characteristic of RA patients. Lacosamide, originally created as an antiepileptic medication, has demonstrated effectiveness in treating seizures and neuropathic pain. It is currently undergoing phase III clinical trials for epilepsy and neuropathic pain. Studies indicate that lacosamide can reduce heightened sensitivity to pain in animal models, such as carrageenan-induced inflammation and arthritis-related pain. This suggests its potential to address different types of inflammatory pain, both acute and chronic, in human patients (17). Study conducted by Tirmizi et al. (18) supported present study outcome, in such a way that leflunomide was mostly given to RA patients than Methotrexat, and also considered that leflunomide had been more effective in treatment of RA compared to methotrexate.

Conclusion

The study concluded that there is high prevalence of RA in twin cities, Rawalpindi and Islamabad, Pakistan. Female compared to male are much more affected by this disorder which is due to lack of exercise and less physical activity. Further, high number of patients with RA were aged above 60 years old as well as had higher BMI. Many patients were diagnosed by RF test and lacosamide and leflunomide had been prescribed more than hydrochloroquine and Methotrexate. Patients were recommended to monitored disease activity regularly and gentle exercise that can help in strengthening muscles and joints.

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