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Demographic features, Challenges, and Treatment Outcome of Rheumatoid Arthritis patients in Private Healthcare System in a Low-income Country

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Abstract

Objectives

In a low-income country like Bangladesh; the study was taken place in a private rheumatology center between 1st January 2016 to 31st December of 2016 includes 85 Rheumatoid Arthritis (RA). The aim of the study was to observe and statistically analyze the response to treatment with different types of disease-modifying antirheumatic drugs (DMARDs). Initially the patients were treated with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) like Methotrexate (MTX), Leflunomide (LEF), Sulfasalazine (SSZ) and Hydroxychloroquine (HCQ). Since the biological disease-modifying antirheumatic drugs were expensive and not affordable by most of the refractory to csDMARDs patients, these patients were treated with a single Janus kinase (JAK) inhibitor; a targeted synthetic (tsDMARD) TOFA (TOFA) when the drug available in Bangladesh in July 2016. Treatment response was assessed by use of disease activity score of 28 joints (DAS28) using Erythrocyte Sedimentation Rate (ESR) and C-Reactive Protein (CRP). The adverse effects of different DMARDs, patients' residence (urban or village) with their monthly income; lastly attendance rate of the patients for timely follow-up were assessed.

Methods

An observational, prospective cohort study was performed. After obtaining the informed consent of individual patient; history taking, direct clinical examination, interview of the patients and clinical disease activity, adverse effects etc. were recorded and statistically analyzed.

Results

The mean age at diagnosis was 40.68±13.56 years; mostly females (n=69, 81.18%). Majority of the patients had obtained post-primary education (n=67, 78.82%). Two-third patients (n=66, 77.65%) were house wives; funded by their husbands. Majority of the patients (n=73, 85.88%) had moderate to severe impairment of activities of daily living (ADL) at the time of enrollment with moderate to high disease activity. Most of the patients (n=77, 90.59%) had a positive rheumatoid factor test at recruitment and considerable number of patients (n=53, 62.35%) had a positive anti-cyclic citrullinated peptide (ACPA) test. Eighteen patients (21.18%) were in remission with DAS28 score <2.6 and 54 patients (63.53%) could achieve low disease activity with DAS28 score between 2.6-3.2. The adherence rate was much satisfactory as high (18.82%), moderate (75.29%) and non-adherent (5.88%) respectively.

Conclusions

Many a times, the RA patients could not achieve lower rate of remission or low disease activity that need expensive biological treatment that a few patients in Bangladesh can afford. The emergence of Janus kinase (JAK) inhibitor; TOFA helped those patients to achieve at least low disease activity. This small study has shown higher adherence to medication/s and timely follow-up and treatment with TOFA results in both lower disease activity and functional disability with a better expected remission.

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Key Words: Conventional Synthetic and Targeted Synthetic Disease Modifying Anti-Rheumatic Drugs, Disease Activity Score, Remission

Introduction

Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disease characterized by persistent synovitis and progressive joint destruction and disability. Early diagnosis and treatment prevents the joint deformities, impaired function and disability.[1] According to available existing guidelines and recommendations, the conventional synthetic (cs) disease-modifying antirheumatic drugs (csDMARDs) like MTX, LEF, SSZ) and HCQ while MTX is the first-line csDMARDs.[2]

We follow the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) have jointly developed new definitions for remission that provide an optimal clinical outcome. The attainment of remission according to these criteria likely to prevent joint destruction or minimizing the progression of joint damage irrespective of residual subclinical changes that helped the patients to achieve better physical function, improved quality of life and work capacity and reduced comorbidity risks.[3]

Material and Methods

An observational, prospective cohort study was performed conducted in a private rheumatology consultation center at Dhaka, Bangladesh, reviewing clinical history, clinical examinations and medical records of 85 RA patients, those fulfilled the 2010 Rheumatoid arthritis classification criteria of an American College of Rheumatology/European League Against Rheumatism[4] collaborative initiative treated by rheumatologists at a private hospital between 1st January 2016 to 31st December 2016.

The demographic variables such as gender, age of onset of arthritis, mean age at the time of the consultation, diagnosis of RA (years), RA duration and follow-up time (in months) are recorded. Besides these, the DAS28 'disease activity score' was the tool to measure of disease activity in RA patients. The DAS28 are recorded and compiled for analysis. The autoantibodies like Rheumatoid Factor, Anti-CCP and Rose-Waaler tests were carried out. The study included RA patient's ≥ 18 years that were initially put on csDMARDs (MTX, SSZ, LEF, HCQ) sequentially as per existing guidelines either due to nonresponding or due to adverse effects. The patients who were refractory to different csDMARDs were treated with tsDMARDs (TOFA). The pregnant or lactating female patients, children, or immune compromised patients were excluded from the study. Written informed consent was obtained from each patient enrolled in the study. The patients were followed-up initially at an interval of 4-6 weeks; then at 12-week interval with the recording of disease activity by DAS28.

Study Population and Selection Criteria

The study population included patients presenting to the Private Rheumatology Center, and with a definite diagnosis of RA based on American College of Rheumatology (ACR) or ACR/ European League Against Rheumatism (EULAR) criteria (score ≥6).

Inclusion Criteria

This study included patients with the following:

Definite diagnosis of rheumatoid arthritis as per ACR or ACR/EULAR criteria (score ≥6)

Aged 18 years and above

Consented to participate in the study

Moderate to high disease activity index.

Exclusion Criteria

The pregnant or lactating patients and patients who declined to consent to participate in the study and those too ill to participate in the study at the time of data collection were excluded.

Statistical Analysis

All these results were calculated, and compared using statistical analyses, where necessary both continuous variables or categorical variables were expressed as Mean ± SD.

Results

Total 85 RA patients were enrolled and assessed.

Clinical characteristics

At time of reporting to us, apart from symmetrical inflammatory polyarthritis affecting more markedly in upper limb small joints, as presenting features (Table 1), more than half of the patients had impairment of activities of daily living (ADL) that affects their daily routine life. Next remarkable features are low grade fever or feverish feeling and fatigue. Nearly a third patient presented with morning stiffness of the affected joints (Table 1) & (Table 2).

A little number of patients presented as palindromic features and initially treated with HCQ though most of these patients had to be treated with other DMARDs mostly with MTX. The MTX was the anchor drug and around fifty percent patients were treated with this drug though other csDMARDs were also used as mono therapy (Table 3). However, many patients had to be treated either with SSZ or LEF due to either due to refractory to MTX or due to its adverse effects (Table 4). Partial responded patients being treated with MTX were treated with the combination of SSZ or HCQ. Few patients were managed with so-called triple-therapy with MTX, SSZ & HCQ. Unfortunately, little more than thirty percent patients did not response to triple-therapy and being treated with TOFA (tsDMARD) with a considerable remission rate (Table 3) & (Table 4).

At the last quarter of the study, after the launching of TOFA (tsDMARD) in July 2016 in Bangladesh, there was dramatic reduction of disease activity achieved that lead to higher rate of remission rate or low disease activity (Table 5) & (Table 6) attained.

Socio-demographic characteristics

Statistical analyses showed that mean age at diagnosis is around forty; out of which most of the patients were house wife (Table 6) and other parameters also shown. The patients in the age group of 50-59 years were significantly higher as compared to those in the groups <49 ($p<0.0001$) and ≥60 ($p<0.0001$). There was no statistically significant difference between the population in the groups 40-49 and 50-59 ($p>0.05$). The female patients show statistically higher significant difference ($p<0.0001$) than male patients (Table 7).

Discussion

Currently approximately 1% of the worldwide population suffers from RA that is one of the most common autoimmune diseases. The disease causes both local and systemic bone loss, resulting in joint destruction and increased fracture risk. Immune responses against citrullinated proteins are a key player in the development RA in the patients suffer from RA.[5]

In our study, RA was found most of patients are females with a male to female ratio of 1:4.31. The range of age of patients were between 22 to 76 years of age most of the enrolled patients presented with moderate to high disease activity (DAS28 score >3.3; even some were >5.1). Dramatic improvement found in the disease activity after the patients were being treated with Janus kinase (JAK) inhibitor; TOFA .

The most of the patients complains of morning stiffness with swollen and tender joints though nearly half of the patients do not complain of morning stiffness.[6]

Poor adherence to medication in patients with rheumatoid arthritis is found in most of the studies with range of from 30 to 80%[7]. Arshad et al. have shown that higher medication adherence with RA exhibits achievement of lower disease activity during treatment and better outcome with DMARDs.[8,9]

Previous study confirmed that treatment with TOFA in patients with moderate to severe RA resulted in greater remission and low disease activity rates.[10]

Similarly, in our small study, patients' better adherence to treatment and follow-up schedule resulted in better outcome including remission or low disease activity though significant improvement noticed with tsDMARDs (TOFA).

Conclusion

Many a times, the RA patients could not achieve lower rate of remission or low disease activity that need expensive biological treatment which is only affordable by a few patients in Bangladesh. The emergence of Janus kinase (JAK) inhibitor; TOFA helped those patients to achieve at least low disease activity. Well-educated patients on the disease could achieve and maintain remission that will certainly benefit them substantially both physically and economically. This small study has shown higher adherence to medication/s and timely follow-up and treatment with TOFA results in both lower disease activity and functional disability with a better expected remission.

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Ethical Responsibilities

The authors declare that this study did not perform experiments on humans or animals.

The authors declare that they have followed the protocols of their professional private practicing place regarding the publication of data from patients, all the patients included in the study have received sufficient information and gave written informed consent to participate in the study.

Limitation of the Study

A small cohort study may not accurately represent the true distribution of characteristics within the larger population. So, the study has limitation to apply the study's findings to other individuals or situations.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

Tables

Table-1: Presenting features of study participants

Unintentional weight loss n (%)	20 (23.53)
Asthenia n (%)	5(5.88)
Fatigue n (%)	45(52.94)
Myalgia n (%)	15(17.65)
Morning stiffness more than one hour n (%)	33(38.82)
Impairment of activities of daily living (ADL) n (%)	73(85.88)
Palindromic pattern n (%)	13(15.29)
Low grade fever or feverish feeling n (%)	35(41.18)
Dry eye n (%)	5(5.88)
Red eye n (%)	5(5.88)
Dry cough n (%)	15(17.65)
Carpal tunnel syndrome n (%)	35(41.18)

Serologically most of the patients are seropositive (both RA factor and ACPA) (Table 2) though small number of patients are seronegative

Table-2: Serological status and disease activity indices of study participants

Rheumatoid factor (n, %)	Positive	77 (90.59)
	Negative	8 (9.41)
ACPA (n, %)	Positive	53 (62.35)
	Negative	32 (37.65)
Rose-Waaler Test* (n, %)	Positive	22 (25.88)

*Carried out when Rheumatoid factor and ACPA (Anti-cyclic citrullinated peptide) both were negative

Table-3: The distribution of frequencies of monotherapy treatment in patients with RA

DMARDs	Number of patients	%n=85
MTX	43	50.59
SSZ	15	17.65
LEF	22	25.88
TOFA	31	36.47

DMARDs: Disease-Modifying Anti-Rheumatic Drugs

Table-4: DMARDs induced adverse drug reactions

DMARDS	Number of patients	%n=85	Adverse drug reactions
HCQ	3	3.53	Retinopathy
MTX	17	20	Alopecia, Raised transaminases, Cytopenia, Macrocytic anemia
SSZ	11	12.94	Anorexia, Allergic reactions
LEF	9	10.59	Alopecia, nausea, skin rashes
TOFA	3	3.53	Mycosis, opportunistic infections

Table-5: Disease activity

Disease activity (n, %)	Remission (DAS28 score <2.6)	18 (21.18%)
	Low disease activity (DAS28 score 2.6-3.2)	54 (63.53%)
	Moderate disease activity (DAS28 score 3.3-5.1)	8 (9.41%)
	High disease activity (DAS28 score >5.1)	5 (5.88%)

The adherence rate was at a large satisfactory as shown (Table 6).

Table-6: Adherence rate

Adherence (n, %)	High	16 (18.82%)
	Moderate	64 (75.29%)
	Non	5 (5.88%)

Table-7: Age and sex distribution, education level, occupation, place of residence and monthly income

Characteristic	**Total**	
Sex distribution (n, %)	Female	69 (81.18%)
	Male	16 (18.82%)
Age at diagnosis (years; mean, SD)		40.68±13.56
Age groups presented at the treating center (n, %)	<40 years	13 (15.29%)
	40-49 years	24 (28.24%)
	50-59 years	32 (37.65%)
	≥60 years	16 (18.82%)
Education level (n, %)	Primary school	18 (21.18%)
	High school	19 (22.35%)
	Higher secondary school	12 (14.12%)
	Secondary school certificate	13 (15.29%)
	Graduate	13 (15.29%)
	Post-graduation	10 (11.77%)
Occupation (n, %)	Student	5 (5.88%)
	Housewife	66 (77.65%)
	Businessmen	9 (10.59%)
	Professional Job Holder	5 (5.88%)
Place of Residence (n, %)	Urban	50 (58.82%)
	Village	35 (41.18%)
Income* (n, %)	BDT 15000-29999	13 (15.29%)
	BDT 30000-44999	38 (44.71%)
	BDT 45000-59999	21 (24.71%)
	BDT >60000	13 (15.29%)

*BDT: Bangladeshi Taka

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