ORIGINAL ARTICLE

Treatment Outcome of Ankylosing Spondylitis in Srinagarind Hospital

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Background: Ankylosing spondylitis (AS) is a chronic inflammatory disease. The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Ankylosing Spondylitis Disease Activity Score (ASDAS), Visual analog scale (VAS), ESR (erythrocyte sedimentation rate), and CRP (C-reactive protein) are the tools for assessing disease activity.

Objective: The purpose of the present study was to determine the treatment outcome of AS patients in the Rheumatology clinic at Srinagarind Hospital.

Materials and Methods: AS patients who were follow-up between 1 January 2015 and 31 December 2019. The primary outcome was the disease activities by BASDAI, and ASDAS at the initial treatment and the last visit. Moreover, the factors consisting of age, duration of disease, and duration of DMARDs (Disease-Modifying Antirheumatic drugs) used were evaluated for the correlation of persistent high disease activity (BASDAI ≥4 or ASDAS ≥2.1) in patients after treatment.

Results: A total of 42 AS patients consist of 31 males (73.80%). The average age was 41 years old, and the average duration of disease and the duration of DMARDs used were 9.32 and 9.02 years, respectively. Biologic DMARDs used were 6 (14.28%). At the first visit, there were high disease activities patients with BASDAI ≥4; 9 (21.43%), ASDAS ≥2.1; 34 (80.95%) and low disease activities patients with BASDAI <4; 32 (76.19%), ASDAS <2.1; 6 (14.29%). At the last visit, there were high disease activities patients with BASDAI ≥4; 4 (9.52%), ASDAS ≥2.1; 21 (50.00%) and low disease activities patients with BASDAI <4; 37 (88.10%), ASDAS <2.1; 18 (42.86%). The high disease activities patients decreased by 55% after treatment by BASDAI score and decreased by 38% by ASDAS score. Low disease activities group of patients were associated with the use of biologic DMARDs. The correlation of high disease activity to age, duration of disease, and duration of DMARDs used were not significant p-values=0.79, 0.92 and 0.92, respectively.

Conclusion: Most of AS patient can achieved BASDAI goal after treatment.

Keywords: Ankylosing spondylitis; BASDAI; ASDAS; VAS; ESR; CRP; DMARDs

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Ankylosing spondylitis (AS) is a chronic, progressive inflammatory disease that predominantly affects the spine. The main clinical features are chronic inflammatory back pain and progressive spinal stiffness. In severe cases AS causes impaired spinal mobility, and postural abnormalities. Other symptoms include buttock pain from sacroiliitis, peripheral arthritis, enthesitis, uveitis, and dactylitis[1].

The objectives of treatment are relieving pain, recovery of physical activity, and delaying structural damage. Nonsteroidal anti-inflammatory drugs (NSAIDs) are first-line therapy for symptomatic AS patients. Corticosteroids and Disease-modifying antirheumatic drugs (DMARDs) were used for patients who were intolerant to, refractory of, or had a contraindication to NSAIDs treatment.

Biologic DMARDs are becoming increasingly welcome worldwide because of their advantages of acting speed and efficacy over traditional pharmacies in treating AS. Biologic DMARDs are still the agent to treat AS after the failure of conventional therapeutic approaches with NSAIDs, DMARDs, and local or systemic corticosteroids[2].

Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Ankylosing Spondylitis Disease Activity Score (ASDAS), Visual analog scale (VAS), Erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) are the tools for assessing disease activity and also evaluating treatment outcomes of AS. In practical management, BASDAI and ASDAS were wildely used to assess the

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severity of AS. BASDAI is a subjective score of disease activity recorded by patients on their interpretation of disease severity compiled from multiple factors. A score of four or more is thought to be significant and one that requires better disease control[3]. Different from BASDAI, ASDAS is a composite disease activity instrument that incorporates both objective inflammatory markers such as C-reactive protein (CRP) and Patient-reported outcomes (back pain, duration of morning stiffness, patient global assessment, and peripheral joint pain)[4].

The present study aimed to assess the treatment outcome of AS in Srinagarind Hospital. This assessment will benefit the physicians to choose and improve AS treatment.

Materials and Methods

Participants

The present study was a retrospective cross-sectional study design. The 42 AS patients were diagnosed based on ASAS classification criteria or 1984 Modified New York Criteria for AS and age above 18 years old. All patient's demographic characteristics were collected such as age, gender, comorbidities, disease duration, time of DMARDs use, extra-articular manifestations, HLA-B27 status, x-ray grading, History of steroid used, type of conventional and biologic DMARDs, and side effect from medical treatment.

The primary outcome was comparing the disease activities by BASDAI, and ASDAS at the time after the patients obtained an initial treatment period of at least 6 months to the last visit. Moreover, the factors consisting of age, duration of disease, and duration of DMARDs used were evaluated for the correlation of persistent high disease activity (BASDAI ≥4 or ASDAS ≥2.1) in patients after treatment. The present study has been approved by the ethics committee of Khon Kaen University HE631625.

Data collection

Data were collected from patients who attended the Rheumatology clinic between 1 January 2015 and 31 December 2019.

Operational definition

The diagnosis of Ankylosing spondyloarthritis (AS) is based on either ASAS classification criteria or 1984 Modified New York Criteria for classification of Ankylosing spondyloarthritis. ASAS classification criteria for Axial spondyloarthritis diagnosis in a patient with a history of chronic back pain (at least 3 months duration) that began before 45 years of age, with or without peripheral symptoms[5]. Modified New York criteria the criteria include radiological criterion plus 2 of the 3 clinical criteria of the following: Clinical criteria (a) Low back pain and stiffness of at least 3 months duration improved by exercise and not relieved by rest (b) Limitation of motion of the lumbar spine in both the sagittal and the frontal planes (c) Limitation of chest expansion relative to values normal for age and sex. Radiological criterion: Bilateral sacroiliitis grade ≥II or unilateral sacroiliitis grade III to IV[6]. Disease-modifying anti-Rheumatic drugs (DMARDs) are immunomodulatory agents which are classified as either conventional DMARDs or biologic DMARDs. Commonly used conventional DMARDs include sulfasalazine, methotrexate, and leflunomide. Biologic DMARDs are usually prescribed after the failure of conventional DMARDs therapy (ongoing disease activity or clinical or radiographic disease progression). Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Ankylosing Spondylitis Disease Activity Score (ASDAS), and Visual analog scale (VAS) are the instruments for defining disease activity in ankylosing spondylitis (AS). The high disease activity is defined as Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) ≥4 or Ankylosing Spondylitis Disease Activity Score (ASDAS) ≥2.1[7].

Statistical analysis

The descriptive statistics were used suitably. Qualitative variables were described by frequency and percentage. Quantitative variables were described by means and standard deviations. The correlation between factors and persistent high disease activity (high disease activity at the last visit period) was analyzed by Pearson correlation. A p-value of less than 0.05 was considered statistical significance. SPSS version 26 was used for all analyses in the present study.

Results

Clinical characteristics of the patients

During the study period, we identified 42 AS patients consisting of males 31 patients (73.80%), and females 11 patients (26.20%). The average age was 41 years old, The average body weight and height were 62.8 kg and 166.17 cm, respectively. HLA B-27 was detected in 22 patients (52.38%). The average duration of disease and the duration of DMARDs used were 9.32 and 9.02 years, respectively. Sulfasalazine was a conventional DMARDs mostly used in 16 patients (38.10%). Biologic DMARDs used were on 6 patients (14.28%). The details of baseline characteristics are provided in Table 1.

Primary outcome

Disease activity and marker in the initial treatment period and last visit treatment period

The disease activity indices of the initial treatment period and the last visit treatment period are shown in Table 2.1 and 2.2. In Table 2.1, in the initial treatment period,

Table 1. Baseline characteristics

Patient characteristics	n=42, n (%)	Percent
Gender		
Female	11	26.20
Male	31	73.80
Age (year, mean/SD)	41 (11.06)	-
BW (kg, mean/SD)	62.80 (13.43)	-
Height (cm, mean/SD)	166.17 (1.26)	-
BMI (kg/m^2)	22.7 (4.39)	-
HLA B-27		
Positive	22	52.38
Negative	4	9.52
No data	16	38.10
Comorbidities		
Hypertension	9	21.42
Diabetic Mellitus	4	9.52
Dyslipidemia	9	21.43
CKD	1	2.38
AVN	4	9.52
Osteoarthritis	2	4.76
Osteoporosis	1	2.38
Thalassemia	3	7.14
Old TB	2	4.76
Others	11	26.20
None	14	33.33
Disease duration (year, mean/SD)	9.32 (4.23)	-
Time of DMARDs used (year, mean/SD)	9.02 (4.15)	-
Extraarticular manifestation		
Sleep disturbance	3	7.14
Acute anterior uveitis	3	7.14
Inflammatory bowel disease	1	2.38
None	35	83.34
Sacroiliitis plain radiograph grading		
Grade 0	1	2.38
Grade 1	1	2.38
Grade 2	9	21.42
Grade 3	27	64.30
Grade 4	4	9.52
Steroid use		
Yes	4	9.53
No	38	90.47
DMARDs		
Methotrexate	2	4.76
Sulfasalazine	16	38.10
Methotrexate + Sulfasalazine	12	28.58
Methotrexate + Azathioprine	2	4.76
Methotrexate + Cyclosporin A	1	2.38
Sulfasalazine + Azathioprine	1	2.38
Sulfasalazine + Etanercept	2	4.76
Methotrexate + Sulfasalazine + Azathioprine	1	2.38
Methotrexate + Sulfasalazine + Leflunomide	1	2.38
Methotrexate + Sulfasalazine + Etanercept	2	4.76
Sulfasalazine + Leflunomide + Etanercept	1	2.38
Methotrexate + Sulfasalazine + Azathioprine + Etanercept + Infliximab	1	2.38
Side effect		
Acute kidney injury	1	2.38
Rash	3	7.14
Hepatitis	3	7.14
Upper GI bleeding	1	2.38
Gastroesophageal reflux disease	1	2.38
Others	2	4.76
None	28	66.67

BW=body weight; BMI=body mass index; CKD=chronic kidney disease; AVN=avascular necrosis; TB=tuberculosis; DMARDs=Disease-Modifying antirheumatic drug

High disease activity by the BASDAI score was found in 9 patients (21.43%) and the ASDAS score was found in 34 patients (80.95%). In the last visit treatment period, High disease activity by BASDAI was found in 4 patients (9.52%), and ASDAS was found in 21 patients (50.00%).

In addition, in Table 2.2, VAS was 50.38 mm. (SD 2.96), ESR 53.25 mm/hr (SD 4.40), and CRP 36.51 mg/L (SD 6.69) in the initial treatment period. In the last visit, VAS was 27.49 mm (SD 3.15), ESR was 39.65 mm/hr (SD 4.46), and CRP was 13.30 mg/L (SD 2.39), respectively. The high disease activities patients were decreased by 55% after treatment by BASDAI score (5 from 9 patients) and decreased by 38% by ASDAS score (13 from 34 patients).

Disease activity and biologic DMARDs

The present study found that patients that received biologic DMARDs (6 patients) in the initial treatment period had high disease activity in 4 patients (66.67%) by BASDAI and 6 patients (100%) by ASDAS. In the last visit, 2 patients (33.33%) had high disease activity by BASDAI and 3 patients (50%) by ASDAS. in Table 3.1.

In addition, in Table 3.2, the Clinical response after DMARDs (BASDAI <4 or ASDAS <2.1). In the present study, 6 patients had received biologic DMARDs, which 4 out of 6 patients (66.67%) had clinical improvement. In the 36 patients who recieved only conventional DMARDs, 34 out of 36 patients (94.44%) had clinical improvement.

Secondary outcome

The correlation between factors and high disease activity

No statistical significance between factors and high

Table 2.1. Disease activity by BASDAI and ASDAS in initial and last visit treatment period

Disease activity	Initial treatment n=42, n (%)	Last visit n=42, n (%)
BASDAI		
<4	32 (76.19)	37 (88.10)
≥4	9 (21.43)	4 (9.52)
None	1 (2.38)	1 (2.38)
ASDAS		
<1.3	1 (2.38)	4 (9.52)
1.3 to <2.1	5 (11.90)	12 (28.57)
2.1 to 3.5	27 (64.29)	20 (47.63)
>3.5	7 (16.67)	3 (7.14)
None	2 (4.76)	3 (7.14)
ASDAS		
<2.1	6 (14.29)	18 (42.86)
≥2.1	34 (80.95)	21 (50.00)
None	2 (4.76)	3 (7.14)

BASDAI=Bath Ankylosing Spondylitis Disease Activity Index; ASDAS=Ankylosing Spondylitis Disease Activity Score

Table 2.2. Disease markers in the initial and last visit treatment period

Markers	Initial treatment, mean/SD	Last visit, mean/SD
VAS (mm)	50.38 (2.96)	27.49 (3.15)
ESR (mm/hr)	53.25 (4.40)	39.65 (4.46)
CRP (mg/L)	36.51 (6.69)	13.30 (2.39)

VAS=visual analog scale; ESR=erythrocyte sedimentation rate; CRP=C-reactive protein

Table 3.1. High disease activity and biological DMARDs

Disease severity	Initial treatment, n=6, percent	Last visit, n=6, percent
BASDAI ≥4	4 (66.67%)	2 (33.33%)
ASDAS ≥2.1	6 (100%)	3 (50%)

DMARDs=Disease-modifying antirheumatic drug; BASDAI=Bath Ankylosing Spondylitis Disease Activity Index; ASDAS=Ankylosing Spondylitis Disease Activity Score

Table 3.2. Clinical response after DMARDs treatment (BASDAI <4 or ASDAS <2.1)

Type of DMARDs	Total, n=42	Improve, n (%)	Not improve, n (%)
Biologic DMARDs	6 (14.29%)	4 (66.67%)	2 (33.33%)
Only conventional DMARDS	36 (85.71%)	34 (94.44%)	2 (5.56%)

DMARDs=Disease-Modifying antirheumatic drug

Table 4. Correlation between factors and high disease activity in the last visit treatment period

Factors	p-value
Age	0.79
Disease duration	0.92
Time of DMARDs	0.92
Initial ESR	0.54
Initial CRP	0.86

DMARDs=Disease-modifying antirheumatic drug; ESR=erythrocyte sedimentation rate; CRP=C-reactive protein

disease activity. The data are shown in Table 4. The p-values are 0.79 in age, 0.92 in disease duration, 0.92 in the time of DMARDs used, 0.54 in initial ESR, and 0.86 in initial CRP.

Discussion

There are a large number of disease activities tools of AS. In practical management, BASDAI and ASDAS are wildely used to assess the severity of AS. The goal of treatment is a low disease activity state which was defined by BASDAI <4 and ASDAS <2.1. As the results of our study, we used all of BASDAI, ASDAS, VAS, ESR, and CRP. After the patients were attended to the Rheumatologic clinic. We found that the clinical was improved and decreased the number of high disease activity patients in all the tools' results.

According to Thai Standard management guidelines, this study showed most of the patients achieved their goals by BASDAI (BASDAI <4). However, 50% of patients with ASDAS scores did not reach therapeutic targets, probably from BASDAI is an assessment of the severity of the disease based on the patient's feelings or satisfaction but these patients still have an increase in inflammatory markers that may lead to progressive spinal damage. This result is consistent with previously published research by Byravan et al. 2021[5], which showed that BASDAI is a subjective score of disease activity recorded by patients on their interpretation of disease severity compiled of multiple factors. However, the question arises of whether this subjective assessment correlates accurately to objective inflammation on MRI or if the score is skewed by other patient factors and therefore can it accurately assess disease activity[3].

While ASDAS is a composite disease activity instrument than the BASDAI because it incorporates both objective inflammatory markers such as C reactive protein (CRP), Erythrocyte sedimentation rate (ESR), and patients report outcomes (back pain, duration of morning stiffness, patient global assessment, and peripheral joint pain) as shown in the previous study by Marona et al. 2020[4].

The previously published study by Vastesaeger et al. 2014[7] showed that the patients selected with elevated BASDAI had characteristics associated with more good response to anti-TNF therapy than the patients selected with high ASDAS but in the present study with high disease activity, the patients were improved after biologic DMARDs treatment by BASDAI equal to ASDAS (reduction of 50% in both severity indices).

The present study also showed that there were no factors such as age, disease duration, time of DMARDs used, initial ESR, and CRP were associated with the disease activity responses.

The limitations of our study were the small sample size which may affect the study results and the present study collected data from medical records reviewed only may have some missing data which may affect the results too.

Conclusion

Most of AS patients can achieved BASDAI goal of treatment, however, 50% of the AS patients did not achieve the goal of treatment defined by ASDAS.

Age, duration of disease, duration of DMARDs used, initial ESR, and initial CRP were not correlated to high disease activity responses after treatment.

What is already known on this topic?

The treatment outcome of Ankylosing spondylitis can be measured by various tools. In the light of treating to target, every treating physician tries to control the AS disease activity to an acceptable level or in remission status.

What is this study adds?

The authors explored the outcome of treating AS by using the practical composite score including BASDAI, ASDAS, and other clinical parameters to classify the result of treatment and the factor that influent the outcome.

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Conflicts of interest

The authors declare no conflict of interest.

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