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Impaction of Delay of Diagnosis of Ankylosing Spondylitis Patients on Structural Changes

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ABSTRACT

Background: Ankylosing spondylitis (AS) is an inflammatory condition with prolonged pain that results in loss of function. Diagnosis delay in the past had little effect on the prognosis of AS because of the lack of an appropriate treatment options. It is now possible to reduce the advancement of AS in patients who have had it for a shorter time since biological treatment is highly effective, early diagnosis in AS has become increasingly critical.

Objective: The aim of the work was to determine the relation between delay of treatment for ankylosing spondylitis patients and structural changes by Bath ankylosing spondylitis radiology index (BASRI) as well as Modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS).

Patients and Methods: At Zagazig University Hospitals, the Department of Rheumatology and Rehabilitation, the Faculty of Medicine, 42 patients with Ankylosing spondylitis were studied using the modified criteria of New York for Ankylosing spondylitis. Data were recorded from taking complete history, local as well as general examination and laboratory investigations involved; complete blood picture, kidney function tests, CRP, ESR and complete urine analysis. The radiological progression was assessed by mSASSS, and BASRI.

Results: The present results showed that mean patients age at disease onset and at diagnosis were 23.9, and 35.14 respectively, the mean of diagnosis delay was 7.66 years. There is a significant positive association between period of delay of patients to intake proper treatment and BASRI, and mSASSS ($p<0.05$).

Conclusion: It could be concluded that diagnosis delay of AS is associated with more structural damage detected by mSASSS and BASRI that reflects the importance of early diagnosis.

Keywords: Bath ankylosing spondylitis radiology index, Modified Stoke Ankylosing Spondylitis Spinal Score, Ankylosing Spondylitis

INTRODUCTION

Among inflammatory rheumatic disorders, ankylosing spondylitis (AS) shows the longest diagnosis delay which is the time between symptom onset to a definitive diagnosis as ankylosing spondylitis patient. This delay has a significant effect on patient outcomes and well-being **(1).**

Diagnostic delay in AS was reported a decade ago to be between five and ten years. Diagnostic delay varies according to peripheral arthritis, educational level, extra articular manifestation, sex in addition to family history, as well as Human Leukocyte Antigen B27 (HLA-B27) status **(2).**

Due to the lack of a viable treatment strategy for AS in the past, this lag period in diagnosis had little impact on the disease's outcome **(3).** The disease progression of people with shorter disease duration can now be decelerated by managing the early stages of AS **(4)**. It has become increasingly critical to diagnose AS early because of the availability of highly effective treatments, such as biological treatment **(5)**.

The current study was aimed to assess impaction of delay of diagnosis of ankylosing spondylitis patients on structural changes by mSASSS and BASRI.

PATIENTS AND METHODS

This study included a total of 42 patients with Ankylosing spondylitis, attending at the Department of Rheumatology and Rehabilitation, the Faculty of Medicine, Zagazig University Hospitals. The patients were studied using the modified criteria of New York for Ankylosing spondylitis.

The following diseases were excluded: Overlap syndrome and mixed connective tissue disease, inflammatory bowel disease, reactive arthritis, psoriatic arthritis, malignancies (solid and myeloproliferative), Parathyroid affection, and previous history of fractures as well as patients younger than 18 years.

Data were recorded from taking complete history, local as well as general examination and laboratory investigations involved; complete blood picture (CBC), kidney function tests, CRP, ESR and complete urine analysis.

The radiological progression was assessed by mSASSS, and BASRI.

The mSASSS scoring system depends on the radiographic assessment of the chronic structural changes. The mSASSS ranging between 0 and 72 by the sum of lumbar and cervical of the 24 vertebral edges evaluated by radiographs of lateral vertebral view.

Anteroposterior and lateral lumbar radiographs, as well as lateral cervical radiographs, are used to calculate the Bath Ankylosing Spondylitis Radiology Index for the spine. Lower T12 to upper S1 is a reference point for the lumbar spine, A combination of lateral and anteroposterior radiographs is analyzed, with points

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given to the view that shows the most significant change. To measure the cervical spine, which is defined as the lower C1 to the higher C7, the lateral view is the only to be scored. Grade 0 is considered normal for sacroiliac joints. Grade 1 = Suspicious Grade 2= Sclerosis, some erosions Grade 3= Severe erosions, widening of the joint space, some ankylosis Grade 4 = Complete ankylosis. BASRI score ranges from (2-12) as Adding the lumbar and cervical spine average sacroiliac joint scores yields the result [(6)].

***Ethical Consideration*:**

An approval of the study was obtained from Zagazig University Academic and Ethical Committee. informed consent of all the participants was obtained. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

All data was collected, tabulated, and analyzed using SPSS IBM Corp.'s 2015 edition. It was used to summarise the data using the mean, standard deviation (SD), and median (range) , Quantitative data was expressed in terms of absolute and relative frequencies (numbers) (percentage). To compare two sets of normally distributed variables, the t-test was employed. All of the experiments were conducted in a two-sided fashion. In order to be declared statistically significant, the p-value has to be lower than 0.05 (S). Receiver Operating Characteristics curve displaying true positive rate (Sensitivity) and false positive rate (0-Specificity).

RESULTS

The current study was carried out on 42 ankylosing spondylitis patients. Mean age of patients at disease onset was 23.9, and the mean age at diagnosis was 35.14 and median of age of diagnosis is 35 with range from 19 to 58 years, the mean of diagnosis delay was 7.66 years.

Regarding the clinical characters of ankylosing spondylitis, the median of pain VAS score was 5 and ranged from 0 to 10.

Spinal mobility (median and range) assessed by occiput to wall distance, lateral Lumber flexion; 9(0-18), 9(4-18) respectively, moreover the mean (±SD) Chest expansion of all patients was 3.79±0.76 and Schober`s test, was 12.23±1.52. median of ESR at first hour was 35 with range from 3 to 100 and CRP mg/l had median 10 with range from 0.7 to 108 BASRI had median 8 and range from 2 to 12 and mSASSS had median 24 with range from 3 to 72 (Table 1).

Table (1): Clinical characters of ankloysing spondylitis patients:

Clinical manifestation	
Disease duration / years Median (range)	10(0-25)
Pain VAS Median (range)	5(0-10)
Spinal mobility	
Occiput to wall / cm Median (range)	9(0-18)
Chest expansion / cm Mean± SD	3.79±0.76
Schober`s test / cm Mean± SD	12.23±1.52
Lateral Lumber flexion / cm Median (range)	9(4-18)
Laboratory finding	
ESR Mean± SD	35±7.31
CRP mg/l Mean± SD	10±2.91
Radiological investigation	
BASRI Median (range)	8(2-12)
mSASSS Median (range)	24(3-72)
VAS=visual analogue scale, SD=standard deviation, BASRI=bath ankylosing spondylitis radiological index, mSASSS=modified stoke ankylosing spondylitis spine score , ESR=erythrocyte sedimentation rate , CRP=C-reactive protein	

Regarding clinical manifestation among ankloysing spondylitis patients, 14.4% of patients had GIT as well as eye manifestation. For Pelvic compression, pelvic distraction, Sacral compression, FABER / Gaenslen's test, 35.7%, 28.6%, 40.5%, 52.4% respectively. Sacroiliitis were detected among patients.

Table 2. shows that there was significant positive correlation between period of delay of patients to intake proper treatment and BASRI (Figure 1), mSASSS (Figure 2) ($p<0.05$).

Table (2): Correlation between period of delay ankylosing spondylitis patients to intake proper treatment with BASRI, and mSASSS (n.42):

Parameters	**Period of delay of patients to intake proper treatment**	
	R	P
BASRI	0.393	0.01
mSASSS	0.318	0.04

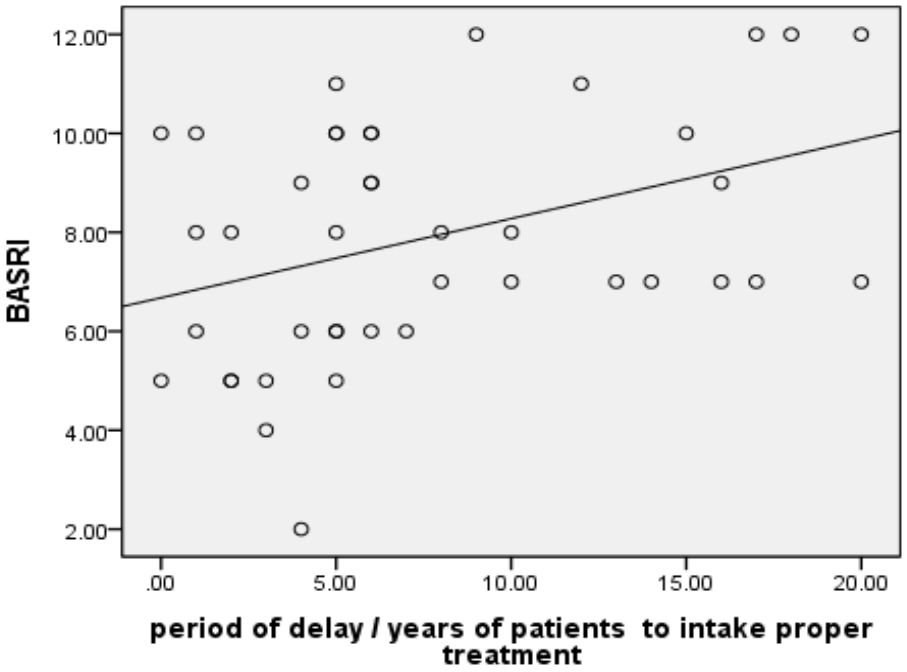

Figure (1): Scatter dot of correlation between period of delay of patients to intake proper treatment and BASRI.

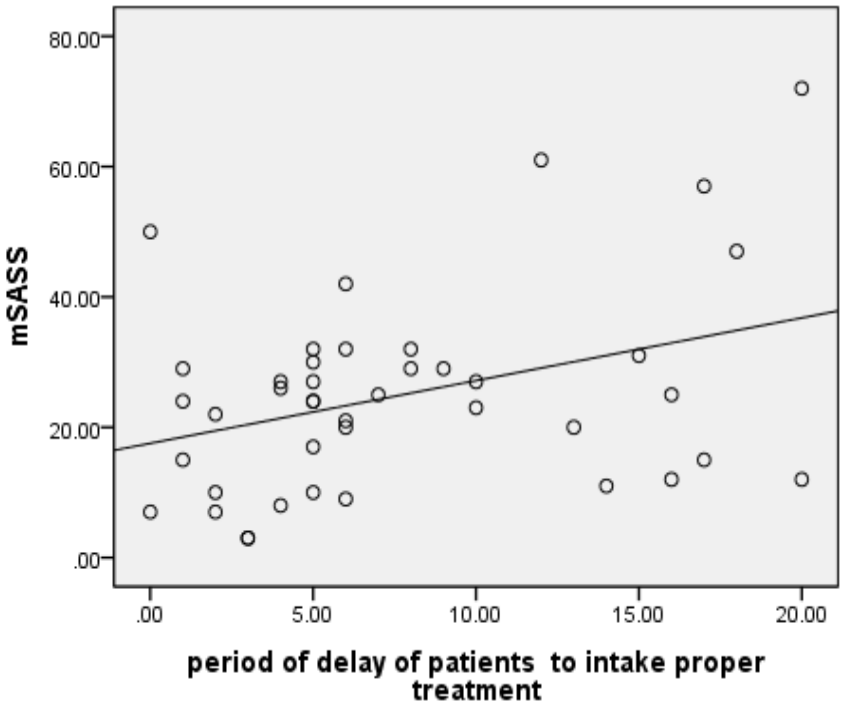

Figure (2): Scatter dot of correlation between period of delay of patients to intake proper treatment and mSASSS.

DISCUSSION

Diagnostic delay is a major challenge in axial spondylo-arthritis which may have impact on different aspects of patient`s life. In the present study, we detect the relation between delay of diagnosis of ankylosing spondylitis and structural changes detected by (BASRI) as well as (mSASSS). We recruited 42 ankylosing spondylitis patients where their mean age at disease onset was 23.9, the mean age at diagnosis was 35.14 and median of age of diagnosis is 35 with range from 19 years old to 58 years old, we found that the mean of diagnosis delay was 7.66 years.

In agreement with our results, study in same department of rheumatology and rehabilitation Zagazig University, **Abdelrahman and Mortada** [(1)] found that (5.7 ± 4.9) years was the average delay in diagnosis. When comparing pre-2010 and post-2010 patients, the mean diagnostic delay is (14±4.4) for patients diagnosed before 2010, and (3.5±1.8) for patients diagnosed after 2010 and a significant difference between both was found (p value<0.0001). The main reason for the delay was a misdiagnosis**.**

In Istanbul, Turkey, at Gulhane Military Medical Academy, **Dincer *et al.*** [(7)] found that the average diagnosis delay was 6.05±5.08 years. where the average age at illness onset was 23.18±9.59, the average age at diagnosis was 27.88±11.63, the average disease duration was 10.44±8.11**.**

Patients from Belgium, France and the Netherlands participated in the outcome in ankylosing spondylitis international study (OASIS) by Ramiro *et al.* with and disease duration of 20.0 (SD 11.6) and a mean age of 42.8 years, CRP was 17.5 (23.5), mSASSS was 10.8 (15.2) and a mean (SD 8.7) of 11 years had passed since the condition was first discovered [(8)].

In harmony with us **Ibn Yacoup *et al.*** [(9)] and **Gurer *et al.*** [(10)] reported that diagnosis of ankylosing spondylitis were delayed on average by 4.12 ± 3.99 years among the 67 male (67 percent) and 33 female (33 percent) patients in the study with average age of the patients at disease onset was 28.56 ± 10.9 years, age (mean ± SD) 38 ± 13 years, average age at diagnosis 32.68 ± 11.56, and mean BASRI score of 6.7 ranging between 2 to 15.

Regarding clinical characters of ankylosing spondylitis our results showed that, the median of pain VAS score was 5 and ranged from 0 to 10. Spinal mobility (median and range) assessed by occiput to wall distance, lateral Lumber flexion; 9(0-18), 9(4-18) respectively, moreover the mean (±SD) Chest expansion of all patients was 3.79±0.76 and Schober`s test, was 12.23±1.52. median of ESR at first hour was 35 with range from 3 to 100 and CRP mg/l had median 10 with range from 0.7 to 108 BASRI had median 8 and range from 2 to 12 and mSASSS had median 24 with range from 3 to 72 .

This was agreed by **Perrotta *et al.*** [(11)] who found that the duration of disease was 12.5 the median (range) pain VAS score was 4.75 (3–5.9), and Median of ESR at 12.5 (5–20.7) mm/h and CRP mg/l had median 0.5 (0.2–0.9) mSASSS had median of 10 with range from 2.5 to 29.5**.**

Also **Salaffi *et al.*** [(12)] found that the mSASSS scores had an average baseline score of 14.4 (± 4.7), with a median of 13 (95% CI for the median, 11-17). There was a median score of 5 for the BASRI-spine scores, with an average baseline score of 6.8 (±3.1) (95 percent CI for the median, 5 - 6.5).

In harmony with us **Baskan *et al.*** [(2)] reported that the BASRI-spine scores had an average score of 7.37± 1.64, with a median of 7 (95% confidence intervals (CI) for median, 7–7.75). The mSASSS scores had an average baseline score of 21.53±10.35, with a median of 18.5 (95% CI for median, 19.13–23.93)**.**

Our study showed that 14.4% of patients had GIT as well as eye manifestation. For Pelvic compression, pelvic distraction, Sacral compression, FABER / Gaenslen`s test, 35.7%, 28.6%, 40.5%, 52.4% respectively. Sacroiliitis were detected among patients.

Also **Perrotta *et al.*** [(11)]**,** reported that the patients with Inflammatory bowel disease, n (%) were 5 (12.5) and Uveitis, n (%) were 9 (22.5). Patients with Sacroileitis IV grade, n (%) were 14 (35) and Sacroileitis II-III grade, n (%) were 26 (65).

While **Fallahi *et al.*** [(13)] showed that among 163 patients with AS, 16 patients were diagnosed with inflammatory bowel disease.

The current results reported a significant positive correlation between period of delay of patients to proper diagnosis and treatment with BASRI, mSASSS (p<0.05).

This was supported by **Ibn Yacoub *et al.***[(9)] who stated that there was a significant difference regarding BASRI between cases with treatment delay less and more than 5 years. Study results demonstrated a good statistically significant link between an increase in diagnostic delay and a higher BASRI score, which is a measure of disease activity and severity.

Our result supported by previous studies by [(13,14,15,16)], they found a significant association between longer diagnosis delay and greater radiographic progression**;** in the remaining study, there was a trend toward greater radiographic progression in patients with longer diagnosis delay, but this difference did not reach statistical significance [(17)]**.**

CONCLUSION

It could be concluded that diagnosis of AS is associated with more structural damage detected by mSASSS and BASRI. This may refer to the importance of early diagnosis of AS.

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