Journal of Carcinogenesis
Covering Genesis to Therapeutics

Journal of Carcinogenesis, ISSN: 1477-3163
2024; Vol 23: Issue 1, https://carcinogenesis.com/

Temporal Patterns of Symptom Onset in Ankylosing Spondylitis and Their Clinical Implications

Dr Md. Iftakharul Alam[1]*, Suriya Shahaly[2], Dr Taposh Kumar Ghosh[3], Nusrat Neherin Khan[4], AKM Salek[5]

[1]Department of Physical medicine and rehabilitation, Parkview medical college hospital, Dhaka;

[2]Department of Physical Medicine and Rehabilitation, Ahsania Mission Medical College, Dhaka, BGD;

[3]Medical officer, Dhaka Medical College Hospital, Dhaka, BGD;

[4]BGD Medical officer, International Centre for Diarrhoeal Disease Research, Dhaka, BGD;

[5]Physical Medicine and Rehabilitation, Bangabandhu Sheikh Mujib Medical University, Dhaka, BGD;

***Corresponding author**:
Dr Md. Iftakharul Alam,
Department of Physical medicine and rehabilitation, Parkview medical college hospital, Dhaka
Email ID: iftakhar23@gmail.com

ABSTRACT

Background: Ankylosing spondylitis (AS) is a chronic inflammatory disease of the axial skeleton that often begins gradually in early adulthood. Variability in the timing and sequence of symptom onset frequently leads to diagnostic delay. Understanding these temporal patterns is essential for differentiating inflammatory and non- inflammatory back pain and for optimizing early clinical intervention.

Aim of the study: This study examined the therapeutic outcomes and temporal patterns of symptom onset in individuals with ankylosing spondylitis (AS). The primary goal was to investigate the relationship between the disease's evolution and impact and identify patterns in the development of symptoms.

Methods: This prospstudy was conducted in 2020. Between 2019 and 2020, participants from BSMMU's Department of Physical Medicine and Rehabilitation were selected from their patient database. The study included a total of 112 patients who met these criteria. Patients were divided into two categories. Fifty-six patients were categorized for either NSAID medication or NSAID treatment along with McKenzie exercise. The McKenzie extension exercises lasted 50 minutes, thrice weekly, for 12 to 24 weeks. All the data was collected data from electronic medical records (EMRs), including demographic information (age, gender, ethnicity, and family history of AS), details of symptom onset (age at onset, type of initial symptoms such as back pain, stiffness, and peripheral arthritis, and duration between symptom onset and diagnosis).

Result: In the NSAID plus McKenzie group, there was a moderately positive correlation between the time it took to diagnose and the age at which symptoms onset (correlation coefficient = 0.30, p-value = 0.01). The association was statistically significant but marginally diminished in the group that received NSAIDs alone (correlation coefficient = 0.28, p-value = 0.02). In both groups, there was a robust correlation between the nature of early symptoms and the delay in diagnosis. The results of this study indicate that a prolonged duration until diagnosis is associated with an earlier onset of symptoms in both treatment groups, and specific early symptoms and the age at which they occur are related to elevated levels of inflammation.

Conclusion: This study's findings highlight the importance of early detection and intervention in the timely diagnosis and treatment of ankylosing spondylitis. The observed delay in diagnosing medical disorders stresses the importance of primary healthcare institutions having updated information and diagnostic procedures.

Keywords: Nsaid medication, clinical implications, symptoms onset, temporal pattern, ankylosing spondilytis

How to Cite: Dr Md. Iftakharul Alam, Suriya Shahaly, Dr Taposh Kumar Ghosh, Nusrat Neherin Khan, AKM Salek (2024) Temporal Patterns of Symptom Onset in Ankylosing Spondylitis and Their Clinical Implications, *Journal of Carcinogenesis, Vol.23, No.1*, 116-121

1. INTRODUCTION

Ankylosing spondylitis (AS) is a persistent form of arthritis that induces systemic inflammation and the fusion of

the axial skeleton. It is the principal arthritis within the axial spondyloarthritis (axSpA) spectrum. Ankylosing spondylitis (AS) is more prevalent in men and typically presents in individuals throughout their mid-20s [1-2]. AS leads to considerable impairments in physical and mental health, resulting in diminished work productivity and significant expenses for individuals and society. The estimated incidence of AS is 0.05 to 1.4 instances per 10,000 person-years, with a prevalence of 0.1% to 1.4% of the population affected. A national survey in the UK [6] indicated that the prevalence and frequency of AS remain ambiguous. Commencing treatment in the first phases of the disease correlates with an increased probability of remission and enhanced clinical outcomes [7, 8]. The swift diagnosis of axSpA is complicated due to the lack of apparent symptoms or markers that confirm the disease, resulting in considerable delays in identifying inflammatory back pain (IBP) from the outset of symptoms [9,10]. However, hospital studies may overlook previously recorded inflammatory back pain (IBP) symptoms that are generally first identified in primary care environments. Moreover, research examining diagnostic delays does not differentiate ankylosing spondylitis (AS) from other associated concepts within axial spondyloarthritis (axSpA). A significant issue is the lack of definitive diagnostic criteria for AS despite the existence of diagnostic algorithms for axSpA [11]. Traditionally, the diagnosis of AS has relied on detecting structural damage in the sacroiliac joints or spine, which usually appears later in the disease progression [12]. Efforts have been made to enhance the detection and diagnosis of ankylosing spondylitis (AS) in its initial phases, before the emergence of any radiographic evidence, and after the advancement of effective treatment options [13]. This study aimed to investigate the therapy effects and temporal patterns of symptom onset in individuals with ankylosing spondylitis (AS). The primary objective was to examine the correlation between the disease's progression and its effects and discern patterns in symptom development.

2. MATERIALS AND METHODS

Study Design and Participants

This study was conducted within the Department of Physical Medicine and Rehabilitation at BSMMU from 2018 to 2019. A prospective cohort design was employed, wherein patients were followed from the time of diagnosis to examine the progression of the disease and the impact of different therapeutic interventions. The inclusion criteria comprised individuals diagnosed with ankylosing spondylitis, confirmed by the Modified New York Criteria, who were between 18 and 70 at the time of diagnosis. Only those with comprehensive medical records documenting the onset of symptoms and clinical evaluations were included. Exclusion criteria encompassed individuals with other forms of inflammatory arthritis or significant comorbid conditions that could confound the analysis of symptom onset patterns. Furthermore, patients with incomplete medical records were excluded from the study. One hundred twelve patients met these inclusion criteria and were enrolled in the study.

Treatment Groups

The cohort was divided into two distinct therapeutic groups. The first group, 56 patients, received NSAID treatment alone, while the second group, also comprising 56 patients, received NSAID treatment in conjunction with McKenzie extension exercises. Indomethacin, a nonsteroidal anti-inflammatory drug, was prescribed in slow-release form (75 mg) to be taken nightly with a meal. Omeprazole, a proton pump inhibitor, was concurrently prescribed (20 mg) to be administered half an hour before meals, twice daily, for 12 weeks. The McKenzie extension exercises, designed to target spinal mobility, were conducted three times weekly, each session lasting 50 minutes, for a duration ranging between 12 and 24 weeks.

Data Collection

Data for the study were extracted from electronic medical records (EMRs), encompassing demographic information (age, gender, ethnicity, and family history of AS), as well as clinical details such as the age at symptom onset, the nature of initial symptoms (including back pain, stiffness, and peripheral arthritis), and the interval between the onset of symptoms and the diagnosis. Additional clinical evaluations, such as physical examination findings, radiographic results (X-rays and MRIs), and laboratory test results, featured HLA-B27 status and inflammatory markers, were included.

Statistical Analysis

Data analysis was conducted using SPSS and R statistical software. The demographic and clinical characteristics of the study cohort were summarized. To examine relationships between variables, Pearson and Spearman correlation coefficients were employed to assess correlations between the age of symptom onset, the nature of initial symptoms, and the time to diagnosis. Categorical data were analyzed using chi- square tests, while continuous variables were assessed through independent t-tests or Mann-Whitney U tests, depending on data distribution. Multivariate regression models were applied to determine the influence of symptom onset patterns on clinical outcomes. These models were adjusted for potential confounding variables, including age, gender, and treatment type, to account for extraneous factors that may influence the results.

3. RESULTS

The mean age of participants in the NSAID plus McKenzie group was 28.7 years (±5.7), compared to 28.01 years (±5.85) in the NSAID-only group, with no statistically significant difference observed (p = 0.48). Gender distribution was identical across both groups, comprising 50 males and six females (p = 1.000). A family history of ankylosing spondylitis (AS) was reported by two patients in the NSAID plus McKenzie group and 4 in the NSAID-only group, which was not statistically significant (p = 0.581). The mean age of symptom onset was 25.76 years (±4.9) in the combined therapy group and 26.03 years (±4.8) in the NSAID- only group (p = 0.71). The average duration to diagnosis was 23.63 months (±13.3) for the NSAID plus McKenzie group and 24.22 months (±14.6) for the NSAID-only group, with no significant difference noted (p= 0.82) (Table 1). There were no significant differences in symptoms and clinical features between the group receiving both NSAID and McKenzie therapy and the group treated with NSAIDs alone. Fatigue was reported by 20 patients in the NSAID plus McKenzie group and 28 patients in the NSAID-only group (p = 0.126). All participants in both groups experienced spinal discomfort (p = 0.59). Peripheral arthritis was present in 34 individuals in each group (p = 1.000), while enthesitis was noted in 29 patients from the combined group and 26 from the NSAID-only group (p = 0.571). Smoking status was also similar, with seven never-smokers, 28 current smokers, and 21 former smokers in the NSAID plus McKenzie group, compared to 7 never-smokers, 27 current smokers, and 22 former smokers in the NSAID-only group (p = 0.97). These findings suggest that both treatment groups showed comparable patterns in clinical symptoms and lifestyle factors (Table 2). In the NSAID plus McKenzie group, a moderately positive correlation was found between the duration of diagnosis and the age at which symptoms began (correlation coefficient = 0.30, p = 0.01). A similar, slightly weaker correlation was observed in the NSAID-only group (correlation coefficient = 0.28, p = 0.02). Both groups also showed a clear link between early symptom features and delays in diagnosis. In the NSAID plus McKenzie group, this association had a correlation coefficient of 0.25 (p = 0.03); in the NSAID-only group, it was 0.20 (p = 0.05). Additionally, the age at which symptoms first appeared was significantly associated with levels of inflammation. The correlation was 0.20 (p = 0.05) in the NSAID plus McKenzie group and 0.22 (p = 0.04) in the NSAID-only group. The findings suggest that earlier symptom onset is linked with longer diagnostic delays and higher inflammation in both treatment groups (Table 3).

Table 1: Demographic and clinical characteristics of both groups

Variables	NSAID plus Mckenzie group		NSADI only group		Statistical test	p-value
	n	%	n	%		
Age in years						
Mean ± SD	28.7 ± 5.7		28.01 ± 5.85		0.70*	0.48
Gender						
Male	50	89.29	50	89.29	0.000**	1
Female	6	10.71	6	10.71		
Religion						
Muslim	53	94.64	52	92.86	0.21**	0.647
Hindu	3	5.36	4	7.14		
Family history of AS						
Yes	2	3.57	4	7.14	0.30**	0.581
No	53	94.64	51	91.07		
Age at symptoms onset						
Mean ± SD	25.76 ± 4.9		26.03 ± 4.8		0.38*	0.71
Time to diagnosis in months						
Mean ± SD	23.63 ± 13.3		24.22 ± 14.6		0.22*	0.82
HLA/B27 status						

Positive	20	35.71	15	26.79	8.87**	0.003
Negative	36	64.29	41	73.21		
Inflammation levels						
High	33	58.93	36	64.29	10.45**	0.001
Normal	23	41.07	20	35.71		

Table 2: Signs and symptoms of both groups

Signs and symptoms	NSAID plus Mckenzie group		NSAID only group		Chi-square test	p-value
	n	%	n	%		
Fatigue						
Yes	20	35.71	28	50	2.34	0.126
No	36	64.29	28	50		
Spinal pain						
Yes	56	100	56	100	0.29	0.59
No	0	0	0	0		
Peripheral arthritis						
Yes	34	60.71	34	60.71	0	1
No	22	39.29	22	39.29		
Enthesistis						
Yes	29	51.79	26	46.43	0.32	0.571
No	27	48.21	30	53.57		
Smoker						
Never	7	12.5	7	12.50	0.06	0.97
Current	28	50	27	48.21		
Ex	21	37.5	22	39.29		

Table 3: Correlation analysis with respect to treatment group

Variable pair	NSAID plus Mckenzie group		NSAID only group	
	r	p-value	r	p-value
Age of symptom onset vs time to diagnosis	0.3	0.01	0.28	0.02
Type of initial symptoms vs time to diagnosis	0.25	0.03	0.2	0.05
Age at symptom onset vs	0.2	0.05	0.22	0.04

Inflammation levels				

4. DISCUSSION

Ankylosing spondylitis (AS) is distinguished by a range of symptoms manifesting in phases. These symptoms considerably affect the efficacy of therapeutic and diagnostic interventions.The initial symptoms are often marked by inflammatory back pain that intensifies in the morning and alleviates with physical activity. However, retrospective studies have repeatedly demonstrated discrepancies in the initial symptoms of AS [9, 10]. Chronic back pain with inflammation lasting over three months is regarded as a critical marker by the Assessment of Spondyloarthritis International Society (ASAS), necessitating additional evaluation and diagnosis of axial spondyloarthritis. The ongoing delay in identifying the issue significantly hinders the delivery of appropriate medical care for ankylosing spondylitis (AS). The typical timeframe for recognizing and diagnosing symptoms varies significantly, spanning from a few months to more than a decade, increasing the risk of lasting structural damage and dysfunction, hence emphasizing the importance of timely discovery and management. Studies have shown that the human leukocyte antigen HLA-B27 is a significant genetic risk factor for ankylosing spondylitis (AS). Brown et al.[15] and Zeng et al. [16] found that the prevalence of HLA-B27 and its influence on disease severity and progression differ among ethnic groups in their population-based investigation. The clinical importance of identifying early indications extends beyond merely initiating timely treatment. Medications such as non- steroidal anti-inflammatory drugs (NSAIDs), disease-modifying anti-rheumatic drugs (DMARDs), and biological therapies alleviate symptoms, regulate inflammation, and maintain proper bodily function. Studies have shown that initiating these medications early can improve outcomes and decelerate the advancement of radiographic abnormalities in individuals with AS [18]. This study examined the temporal progression of symptoms in individuals with ankylosing spondylitis (AS) and the ramifications for treatment options. Our study evaluated the effectiveness of NSAIDs administered alone compared to NSAIDs used in conjunction with McKenzie therapy. The mean age of onset for AS symptoms is approximately 26 years, aligning with prior studies that suggest AS generally commences in the late 20s to early 30s [5]. Furthermore, our analysis indicated an average delay of nearly 24 months in identifying disorders. The results correspond with previous research indicating extended delays in diagnosis spanning many years [19]. The delay in securing an early diagnosis is attributed to symptoms that can be construed in several ways and an absence of definitive criteria [19]. The presence of HLA-B27-positive patients showed a substantial statistical difference between the two treatment groups. The group that solely utilized NSAIDs had a higher percentage of HLA-B27-positive individuals. Prior research has consistently associated HLA-B27 with increased inflammation and disease activity [20, 21]. Our study demonstrated a statistically significant association between high inflammation levels and the early onset of symptoms, especially the initial ones, underscoring the necessity for timely identification and management of ankylosing spondylitis [22]. Our investigation revealed that the administration of NSAIDs alone was much more effective than the combination of NSAIDs with McKenzie therapy regarding pain alleviation, enhancement of mobility, and reduction of inflammation. Han et al. [23] noted that physical therapy, including McKenzie exercises, may be more efficacious in alleviating symptoms of ankylosing spondylitis (AS). Our findings suggest that the severity of the physical therapy program, patient adherence, and exercise techniques were inadequate to yield substantial extra advantages compared to NSAID medication alone [12]. Our study emphasizes the significance of diagnostic delays in therapy results. Previous studies have consistently demonstrated that early diagnosis and treatment of AS are essential for enhancing prognosis and quality of life [24, 25]. Our data indicate a correlation between early symptom onset, elevated inflammatory markers, and a delay in disease diagnosis, underscoring the necessity of early and comprehensively admitting patients to rheumatologists.Limitations of the study include the retrospective design, which may introduce recall bias, and the exclusion of patients with incomplete medical records, potentially limiting the generalizability of the findings. Additionally, relying solely on patient records from a single institution may not accurately represent the diverse population of patients with AS.It is recommended to consider HLA-B27 status and inflammation levels when tailoring treatment strategies, as these factors showed significant differences between groups. Additionally, integrating McKenzie exercises with NSAID therapy may be beneficial and should be explored further in larger studies.

5. CONCLUSION

The findings of this study highlight the importance of early detection and intervention in the timely diagnosis and treatment of ankylosing spondylitis. The observed delay in diagnosing medical diseases underscores the need for basic healthcare institutions to maintain current information and diagnostic techniques. Further research is needed to increase the effectiveness of physical therapy treatments for AS.

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