General Medicine,ISSN:1311-1817, VOLUME 26 ISSUES 3, Page: 1305-13015
Journal link: https://general-medicine.org
Abstract Link: https://general-medicine.org/abstract-1305-1315/
december 2024

Risk factors disease patterns of enclosing spondylitis associated treatment patterns and drug utilization

[1]Dr Faiza Diaz, [2]Dr Saba Ejaz, [3]Dr Nimra Rani, [4]Dr Syed Muhammad Ali Kazmi, [5]Dr Fehmida, [6]Dr Farah Gul

[1]Poonch medical college Rawalakot
[2]Poonch Medical College Rawalakot
[3]Poonch medical college Rawalakot
[4]Azad Jammu and Kashmir medical college Muzaffarbad
[5]Azad Jammu and Kashmir medical college Muzaffarbad
[6]Poonch medical college Rawalakot

Abstract

Objective: The objective of this study is to assess the frequency, and risk factors of ankylosing spondylitis (AS) and its corresponding treatment patterns and drug utilization within the context of real-world clinical practice.

Methods: After the ethical approval from the institutional review board, this cohort study was conducted at Mayo hospital from June 2023 to December 2023. The collected data encompassed various aspects related to the diagnosis of ankylosing spondylitis (AS) by physicians. This encompassed their method of identifying AS, the particular tests and evaluations used to verify the diagnosis, and the demographic and clinical traits of the patients included. The study also analysed the percentage of patients identified as HLA-B27 positive, the time elapsed between the appearance of initial symptoms and the diagnosis of ankylosing spondylitis, the satisfaction of classification criteria, and the treatment strategies employed, such as advanced therapies for controlling AS disease activity.

Results: The mean values for current disease activity and functional index scores were 3.3±2.1 and 1.8±1.09 in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Bath Ankylosing Spondylitis Functional Index (BASFI), respectively. The patients in the study had received treatment with any TNFi for an average period of 3.1±2.1 years. At the time of study enrolment, adalimumab (43%) and Infliximab (27%) were the most frequently utilized TNFi among the four evaluated in this investigation. In the examination of treatment satisfaction, it was observed that the convenience domain had the lowest score (4.2), whereas the scores for side effects, effectiveness, and global satisfaction were 93.7, 75.41, and 73.81, respectively.

Conclusion: Adalimumab was the TNFi most often administered, with Infliximab being the subsequent choice. Adalimumab was administered for the most extended period of time. The use of more accessible treatment choices has the potential to improve overall treatment satisfaction. This research revealed a significant decrease in productivity as a result of AS. In order to include the viewpoints of patients, it is important to give additional consideration to the aspects that are linked to treatment satisfaction and the loss of productivity while making decisions on treatment alternatives.

Keywords: prevalence, risk factors, disease patterns, ankylosing spondylitis

Introduction

Ankylosing spondylitis (AS) is a type of inflammatory rheumatic illness that mostly impacts the axial skeleton [1]. It is characterized by the presence of inflammatory back pain, which subsequently results in both structural and functional limitations and a reduction in overall quality of life. Males exhibit a higher prevalence rate compared to females, with a mean ratio of 3.4 to 1 [2]. Around 80% of individuals experience the initial symptoms of AS before reaching the age of 30, whereas less than 5% of people manifest symptoms after the age of 45 [3]. Due to the compromised physiological functioning experienced by individuals diagnosed with AS, the disease exerts a substantial impact on occupational circumstances. Individuals diagnosed with AS exhibit impairments in various occupational domains, including uninterrupted work performance, prolonged standing, ambulation, sustained focus, interpersonal interactions, and productivity in terms of both quantity and quality, as well as adherence to deadlines. The aforementioned constraints lead to a reduction of production by 6.3% as compared to individuals in good health, or alternatively, an increase in working hours by 7.1% [4]. Given the absence of a cure for AS, the primary objective of treatment approaches revolves around managing symptoms, mitigating joint deterioration, and attaining or sustaining disease remission [5]. Commonly utilized therapeutic interventions encompass non-steroidal anti-inflammatory medicines (NSAIDs), conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), and biologic disease-modifying antirheumatic pharmaceuticals (bDMARDs). Non-steroidal anti-inflammatory medications (NSAIDs) are frequently recommended as the initial therapeutic approach for managing pain and stiffness [4]. In cases where NSAIDs prove to be ineffective, the use of bDMARDs is advocated [6]. This recommendation is supported by significant evidence indicating a prompt and lasting response, particularly in younger patients with a brief duration of the disease, elevated levels of inflammatory indicators, and favorable functional grade [7]. Several biologics, such as adalimumab, secukinumab, infliximab, and ixekizumab, have received approval for the management of AS in patients who have not shown a satisfactory response to NSAIDs. The diagnosis and management of AS involve the involvement of many specialists, such as rheumatologists and orthopedists, who may adopt distinct therapeutic approaches [1]. This study aims to evaluate the incidence, determining factors, treatment approaches, and medication usage related to ankylosing spondylitis (AS) in real-world clinical settings.

Methodology

After the ethical approval from institutional review board, this cohort study was conducted at Mayo hospital from June 2023 to December 2023. Through non-probability consecutive sampling, 200 participants above age 19 years, presenting the symptoms of AS of either gender were included in the present study. Patients below 19 years of age, have any other connective tissue co-morbidity were excluded from the present study. The collected data encompassed various aspects related to the diagnosis of ankylosing spondylitis (AS) by physicians. This encompassed their methodology for diagnosing AS, the particular tests and evaluations used to validate the diagnosis, and the demographic and clinical traits of the patients included. The study also analyzed the percentage of patients identified as HLA-B27 positive, the time between the first symptoms and the diagnosis of ankylosing spondylitis, the satisfaction of classification criteria, and the treatment strategies employed, such as advanced therapies for controlling disease activity in ankylosing spondylitis. The study also evaluated the burden of disease reported by patients with AS, using validated criteria. Participants were asked to voluntarily take part in doing various standard evaluations to determine disease activity, general health status, quality of life (QoL), and productivity. The study analysed the demographic and clinical characteristics of the study participants, together with their treatment regimens. Descriptive statistics for treatment satisfaction (TSQM) and productivity loss (WHO-HPQ) were presented, including frequency (%) for categorical data and mean and standard deviation for numerical data.

Results

Table 1 shows the demographic parameters of the 200 recruited study participants. Mean age of the participants was 52.34±12.32 years, with 67% were males, mean BMI was 25.2±3.5 kg/m2, mean duration of disease was 6.4±3.2 years. About 51% of the participants have high school education, and 79% were employed. The mean values for current disease activity and functional index scores were 3.3±2.1 and 1.8±1.09 in the Bath Ankylosing Spondylitis Functional Index (BASFI) and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), respectively. The patients in the study had received treatment with any tumour necrosis factor inhibitor (TNFi) for an average period of 3.1±2.1 years. At the time of study enrolment, adalimumab (43%) and Infliximab (27%) were the most frequently utilized TNFi among the four evaluated in this investigation. The current TNFi were administered for an average duration of 5.0±1.3 years of adalimumab and 5.3±2.4 years for etanercept. A significant proportion of patients (37%) had been maintained on a low dose, defined as below the permitted dose, in the year preceding their enrolment in the study. In comparison to the other TNFi, adalimumab was administered at a lower dosage in the majority of patients. Approximately 49% of the patients treated with TNFi were given a pen-type device tailored for subcutaneous injection, as shown in Table 2. In relation to concurrent therapies, 26% of the patients utilised conventional disease-modifying antirheumatic medications (cDMARDs), 72% employed NSAIDs, and 26% utilised steroids. In the examination of treatment satisfaction, it was observed that the convenience domain had the lowest score (4.2), whereas the scores for side effects, effectiveness, and global satisfaction were 93.7, 75.41, and 73.81, respectively (Figure 1). Table 3 represent the productivity loss of the study participants with AS.

Table 1: Demographic parameters of the study participants

Demographic parameters	**N=200**
Age (years)	52.34±12.32
Sex, male, n (%)	134 (67%)
Education, n (%)	
High school or less	102 (51%)
College or more	98 (49%)
Employment, n (%)	
Employed	157 (79%)
Unemployed	43 (22%)
BMI (kg/m2)	25.2±3.5
Duration of disease (years)	6.4±3.2
Comorbidity, yes, n (%)	58 (29%)
BASFI, mean (SD)	1.8±1.09
BASDAI, mean (SD)	3.3±2.1
Injection pain, VAS	2±2.12

Table 2: Disease Pattern of the study participants

Parameters	**N=200**
Mean (SD) duration of TNFi therapy from initiation (years)	3.1±2.1
Current TNFi treatments, n (%)	
Infliximab	54 (27%)
Etanercept	40(20%)
Adalimumab	85 (43%)
Golimumab	20 (10%)
Mean duration of current TNFi medication in years	
Infliximab	4.3±2.1
Etanercept	5.3±2.4
Adalimumab	5.0±1.3
Golimumab	3.2±1.9
Number and percentage of doses of the current TNFi therapy administered in the past year per admission	
Approved	127 (63%)
Low	73 (37%)
Infliximab	
>6 mg	20 (37%)
<6 mg	34 (63%)
Adalimumab	
<40 mg	60 (71%)
>40 mg	25 (29%)
Etanercept	
<50 mg	25 (63%)
>50 mg	15(37%)
Golimumab	
<50 mg	2 (10%)
>50 mg	18 (90%)
Mean (SD) BASDAI score categorized by treatment and dosage	
Approved	3.2±2.3
Low	3.4±1.7
Infliximab	
>6 mg	3.3±1.8
<6 mg	2.9±1.5
Adalimumab	
>40 mg	3±1.9
<40 mg	3.7±2.1
Etanercept	
<50 mg	3.4±1.2

>50 mg	3.5±1.90
Golimumab	
<50 mg	3.1±1.2
>50 mg	2.8±1.4
Mean (SD) BASFI score categorized by therapy and dose	
Approved	1.6±1.2
Low	1.5±1.9
Infliximab	
>6 mg	2±2.2
<6 mg	1.3±1.9
Adalimumab	
>40 mg	1.7±1.8
<40 mg	1.5±1.6
Etanercept	
<50 mg	2.3±1.8
>50 mg	2.5±1.2
Golimumab	
<50 mg	2.1±1.2
>50 mg	1.3±1.3
Route of device type, n (%)	
Subcutaneous syringe	54 (27%)
Intravenous	48 (24%)
Subcutaneous pen	98 (49%)
Concomitant use of cDMARD, yes, n (%)	39 (20%)
Concomitant use of NSAID, yes, n (%)	143 (72%)
Concomitant use of steroids, yes, n (%)	52 (26%)

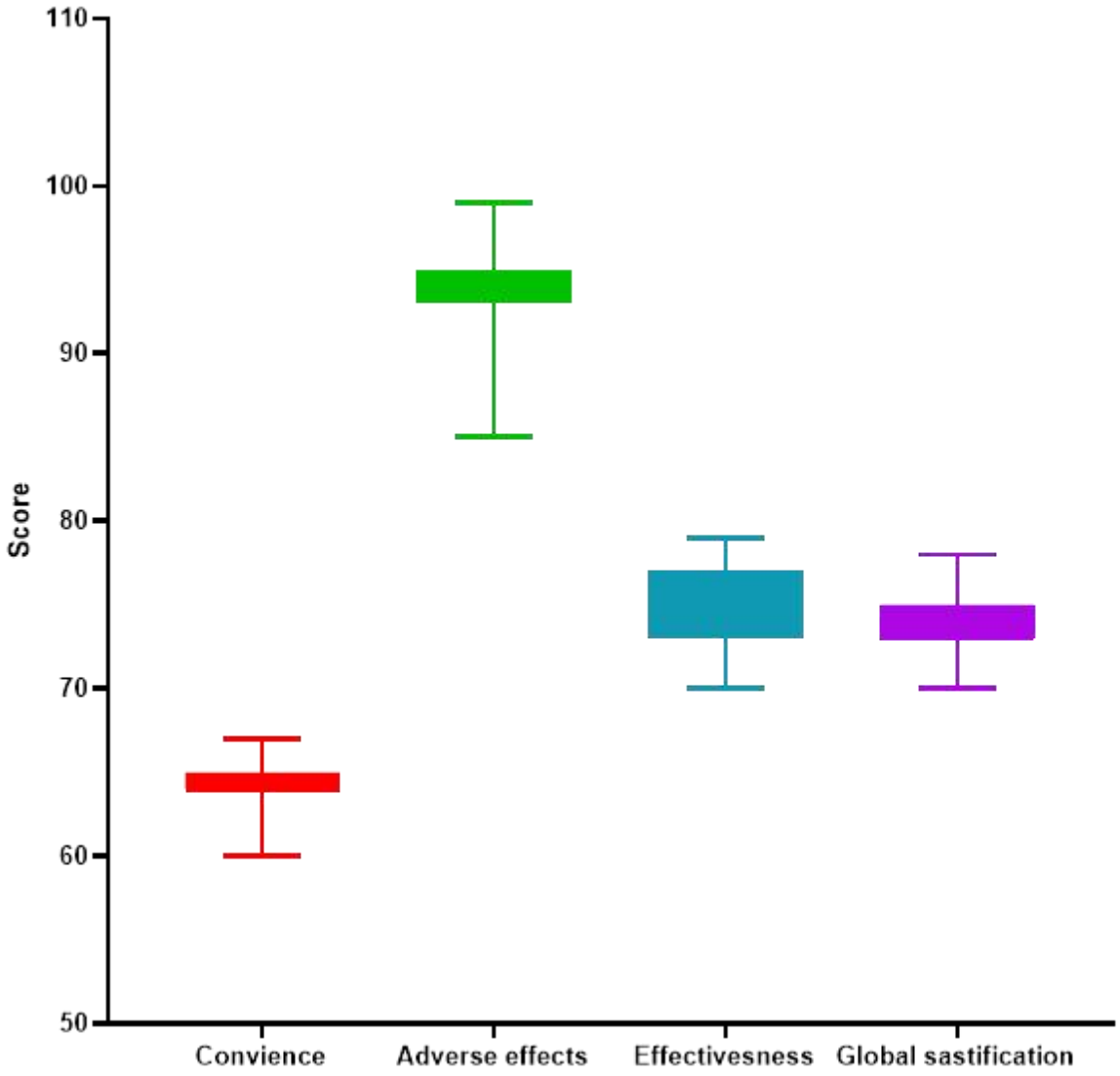

Figure 1: Boxplots depicting treatment satisfaction as assessed by the Treatment Satisfaction Questionnaire for Medication (TSQM)

Table 3: Productivity loss of patients with AS

Parameter	**Mean (SD) (N = 200)**
Days worked if not sick with AS during the last four weeks	24.5±6.2
Number of full days absent from work in the last 4 weeks.	1.2±2.3
Partial absences on work days in the last 4 weeks (days); partial-day absence	1.32±2.6
Self-assessed job performance in the last 4 weeks	6.5±1.5
Productive hours lost due to absenteeism in the last 4 weeks	5.9±24.3
Productive time lost owing to reduced work performance in the last 4 weeks (hours)	54.3±32.2
Hours of lost productivity	55±34.2
Yearly expense due to employee absenteeism in Pakistani Rupees	449242±65430
Yearly expenses due to presenteeism Yearly expenses due to lost productivity (PKR)	3368711±45760
Yearly expenses due to lost productivity (PKR)	3817953±132987

Discussion

Patients in Pakistan with ankylosing spondylitis (AS) who underwent TNFi medication were the subjects of this cohort study, which sought to analyse treatment satisfaction, treatment pattern, and productivity loss. In addition, we investigated the related aspects that help us comprehend the entire disease burden that AS patients face and how TNFi might be practically applied to their treatment. The primary objective of treatment for AS is to mitigate symptoms, enhance and sustain spine flexibility and proper posture, minimize functional impairments, preserve occupational capacity, and mitigate the potential consequences associated with the condition [8]. The effectiveness of TNFi in treating AS has been extensively documented, and their utilization has become an integral part of clinical protocols [9]. Internationally, there exists variation in the utilization of TNFi medications across different countries, as no specific TNFi treatment is universally endorsed over its counterparts. The findings of this study indicate that adalimumab was the most commonly utilized TNFi among the four available options in Pakistan, with Infliximab being the subsequent choice in terms of usage frequency. Sweden and Brazil exhibit a somewhat similar pattern to Pakistan in terms of the frequency of prescribing adalimumab, but etanercept is more typically given in the United States and Canada [10-12]. Tapering of medication dosage is frequently contemplated in clinical practice, taking into account the specific disease activity of each individual patient. In the present investigation, it was observed that around 37% of the participants had been consistently prescribed a low dosage of their current TNFi for a duration of one year prior to their enrolment in the study. The disease activity exhibited by individuals receiving low-dose TNFi treatment were found to be comparable to those observed in patients receiving the recommended dosage of TNFi. Among the TNFi assessed in this study, Adalimumab, specifically, exhibited a longer duration of maintenance and was administered at a lower dosage for a greater percentage of patients. The observed

inclination towards an extended duration of Adalimumab utilization in the present investigation does not aligns with the findings of a prior study conducted in Korea, which demonstrated a prolonged persistence with etanercept as a second-line treatment option for TNFi [13]. This investigation noted the simultaneous use of a tumour necrosis factor inhibitor with conventional disease-modifying antirheumatic medications (cDMARDs) for the treatment of AS, despite the lack of data about the efficacy and safety of cDMARDs in this setting. The European League Against Rheumatism (EULAR) guidelines for the management of AS from 2016 suggest that patients with peripheral arthritis may benefit from this combination medication. [14].

The study found that patient satisfaction with TNFi was much greater than to treatment satisfaction reported for other chronic diseases in Pakistan. It was observed that the convenience domain had the lowest score (4.2), whereas the scores for side effects, effectiveness, and global satisfaction were 93.7, 75.41, and 73.81, respectively. Based on the analysis of TSQM data obtained from prior research, it was observed that individuals diagnosed with postmenopausal osteoarthritis indicated their level of satisfaction with treatment in the domains of effectiveness, adverse effects, convenience, and global satisfaction as 56, 64, 63, and 54, respectively. Similarly, patients with arterial fibrillation who received vitamin K treatment expressed their satisfaction scores as 58, 58, 58, and 56 in the corresponding TSQM domains [15, 16]. In this study, the domain of treatment convenience exhibited the lowest reported satisfaction among the four domains.

In the present investigation, it was observed that individuals participating in the study experienced a mean absence duration of 1.2 full days and 1.3 partial days throughout the preceding four-week period. The findings of this study align with those of a prior investigation conducted on Korean employees, which documented an average of 5.22 hours of work absenteeism resulting from back or neck illnesses. In many research investigations, the concept of productivity loss has been employed as a composite measure encompassing both absenteeism, denoting the act of being absent from work, and presenteeism, which pertains to the effectiveness of work performed by an individual. The reduction in productivity is typically quantified as an annual expense and is referred to as an indirect cost [17]. A systematic review and meta-analysis have documented the costs associated with productivity loss in individuals diagnosed with AS. This comprehensive study identified a total of 32 records that specifically examined the issue of productivity loss in AS patients [17]. The study findings indicate that the yearly indirect expenses associated with reduced productivity in individuals with AS who are undergoing biologic treatment vary between 191 USD and 45,954 USD per individual, based on 2013 USD values [17]. Within the meta-analysis, a study was identified that documented a significant drop in indirect costs subsequent to treatment with a biologic medication. Specifically, the study saw a reduction from an initial value of 1968 USD to a post-treatment value of 191 USD [18]. In our investigation, the yearly expenditure associated with LPT amounted to 3817953±132987PKR. This figure is within the spectrum of previously documented indirect costs in AS and is similar to the expenses incurred by patients in Korea diagnosed with moderate or severe rheumatoid arthritis (moderate: 11,085 USD; severe: 13,157 USD) [19].

There are various limitations inherent in this study. Due to the utilization of a cohort study design in this study, the ability to investigate the causal relationship between factors and patients' reported satisfaction and productivity loss was limited. Moreover, it is important to note that the utilization of self-reported instruments in this study may have introduced variability in the comprehension and interpretation of each item among participants. Despite the aforementioned limitations, it is important to highlight the notable positives of this study. This study employed established and verified metrics that have been extensively

utilized in previous research. Consequently, the findings of this study can serve as a valuable point of reference for comparing results obtained in future studies using the same cohort of participants. Furthermore, this study aims to comprehensively examine the variations in treatment satisfaction, treatment patterns, and expenses associated with productivity loss among patients with Ankylosing Spondylitis (AS) in Pakistan, so contributing to a deeper knowledge of these characteristics within the context of different countries.

Conclusion

After analysing the data, it was found that out of the four TNFi currently used to treat AS in Pakistan, adalimumab is the most frequently given, followed by infliximab. Similar success in regulating disease activity has been seen with the continuous use of adalimumab, usually provided at a modest dose. It seems that adalimumab, even at reduced dosages, can be used in real-world clinical settings and may be sustainable. Among individuals diagnosed with AS, the current TNFi treatment was shown to be quite acceptable. Having said that, happiness was noticeably lower in the treatment convenience domain compared to the other three. Compared to subcutaneous pen injections, subcutaneous syringe and intravenous injections were associated with lower levels of satisfaction. Overall treatment satisfaction might be enhanced by making treatment options more accessible.

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