Original Research Article

A study on comparison of gender-based prevalence and severity at presentation in spondyloarthritis in a tertiary care rheumatic center

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Abstract

Introduction: Spondyloarthritis (or spondyloarthropathy) is the overall name for a family of inflammatory rheumatic diseases that can affect the spine and joints, ligaments and tendons. These diseases can cause fatigue and pain or stiffness in the back, neck, hands, knees, and ankles as well as inflammation of the eyes, skin, lungs, and heart valves. While there is no course of prevention at this time treatment can reduce discomfort and delay the development of spinal deformities.
Aim of the study: The aim of the study was to differentiate gender difference at presentation of spondyloarthritis and to identify markers in determining the severity of disease.
Materials and methods: This was a prospective observational study conducted for a period of 6 months at Institute of Rheumatology, Government K.A.P.V. Medical College and MGM Government Hospital. Totally 62 patients were included in the study 31 males and 31 consecutive females with features of spondyloarthritis per ASAS (Assessment of Spondyloarthritis international Society) at first presentation to our clinic were enrolled and their clinical characteristics were analyzed.
Results: On comparing disease activity and functional indices between males and females, mean BASDAI was 4.66±1.8 versus 4.98±1.94 (p=0.5), mean BASFI was 4.6±2.3 versus 4.8±2.3 (p=0.7),

mean BASMI was3.91±1.94 versus 4.18±2.06 (p=0.4). Out of 31 males, 17 were positive for HLA B27 and 6 out of 31 females were positive for HLA B27 (p=0.04).

Conclusion: The pathogenesis of SpA is multifactorial and not yet fully understood. Genetic factors (HLA-B27 and non– HLA-B27 related genes), inflammatory cytokines (e.g. TNF-alpha, IL-1, IL-6, IL-7, IL-17, and IL-23) and environmental triggers (infections, mechanical stress, abnormal intestinal microbiota) play an important role. These different factors and their complex interaction can lead to activation of autoinflammation and autoimmunity and to the new bone formation. Men are more prone to spondyloarthritis when compared with women.

Key words

BASDAI, BASMI, BASFI, HLA B27, Enthesitis, Dactylitis, Uveitis.

Introduction

The term spondyloarthritis (also known as spondyloarthropathy) covers a group of closely related inflammatory diseases including arthritis of the spine (sacroiliitis or spondylitis) and peripheral joints; as well as inflammation in the area where ligaments and tendons attach to bones (enthesitis or enthesopathy) [1]. These diseases can cause pain in the spine, legs, and arms as joints, ligaments, and tendons become inflamed and/or predispose patients to spinal vertebral fractures. Skin rashes, eye, and intestinal problems can also occur. Diseases that fall under spondyloarthritis umbrella can include: 1) ankylosing spondylitis; 2) reactive arthritis (known previously as Reiter's syndrome) 3) psoriatic arthritis and psoriatic spondylitis, and 4) arthritis or spondylitis associated with the inflammatory bowel diseases, ulcerative colitis, and Crohn's disease [2]. Still, other patients may develop undifferentiated spondyloarthritis. This means they have symptoms or signs of one of the illnesses above, but don't develop the full-blown disease. Like many forms of arthritis, physical therapy and recreational exercise at least 30 minutes per day can significantly improve pain and stiffness [3]. Additional back exercises at least five days per week will also improve pain and function in patients with ankylosing spondylitis [4]. There is also a vast array of drug treatment options for spondyloarthropathy, starting with nonsteroidal anti-inflammatory drugs (NSAIDs), such as naproxen, ibuprofen, Diclofenac or indomethacin given at the outset of the disease symptoms. No one specific NSAID is considered superior to another for spondyloarthritis patients [5]. These in and of themselves will generate considerable relief for patients. Disease-modifying anti-rheumatic drugs (DMARDs) such as sulfasalazine and methotrexate have proven effective in treating accompanying arthritis in the arms or legs, but not for arthritis of the spine or sacroiliac joints. Corticosteroids taken by mouth also can be effective [6]. However, given their side effects, particularly osteoporosis and infections, and new agents now available (see below), these medications are not recommended unless the more effective treatments cannot be used. Injections of depo-steroid medications into joints or tendon sheaths are frequently used by clinicians for symptomatic relief of local flares [7]. Antibiotics such as ciprofloxacin, given over a three-month course soon after disease onset, may have a beneficial effect on the prognosis of reactive arthritis, especially when triggered by Chlamydia trachomatis, but not in other types of spondyloarthritis [8]. Patients with SpA can be distinguished according to their clinical presentation as patients with predominantly axial SpA or with predominantly peripheral SpA. 1 For patients with predominant axial disease the Assessment of Spondyloarthritis international Society (ASAS) has recently developed and validated new classification criteria for axial SpA covering patients with non-radiographic and radiographic axial SpA [9].

Materials and methods

This was a prospective observational study conducted for a period of 6 months from July2018-October 2018 at the Institute of Rheumatology, Government K.A.P.V. Medical College and MGM Government Hospital. Totally 62 patients were included in the study 31 males and 31 consecutive females with features of spondyloarthritis per ASAS (Assessment of Spondyloarthritis international Society) at first presentation to our clinic were enrolled and their clinical characteristics were analyzed. Patients with age of onset <16 years, HIV positive patients, patients previously managed outside for spondyloarthritis and subsequently referred here were excluded. A total of 96 males and 31 females were included, out of the 96 males, 31 males were randomly picked up with software and included for comparison with 31 females. The demographic parameters, symptoms, signs, BASDAI, BASMI, BASFI, HLA B27 were recorded and compared between the two groups. Axial manifestations were defined by the involvement of sacroiliac joints or spine by x-ray or by magnetic resonance imaging. Enthesitis points were taken as per MASES (Maastricht Ankylosing Spondylitis Enthesitis Score Assessment Criteria). A detailed ophthalmological evaluation was done for patients with visual symptoms. Colonoscopy and histopathological examination were done in symptomatic patients.

Statistical analysis

Statistical analysis was performed using the STATA12 software. Descriptive analysis was made for the epidemiological and analytical variables. The differences in parameters between the two groups were analyzed with Student t-test and Mann-Whitney U test. Categorical parameters were analyzed with the chi-square test. A p value of <0.05 was considered significant.

Table – 1: Clinical findings among both the genders with gene expression.

Features	Males n=31	Females n=31	p value
Age at presentation, mean(years)	30.9±8.6	36.8±9.8	0.007
Time lag to first clinical visit, median (months)	24 months	12 months	0.012
Axial manifestations	27(87%)	18(58%)	0.001
Peripheral arthritis	13(41.9%)	26(83.8%)	0.0001
Enthesitis	13(41%)	13(41%)	1
Dactylitis	1(3.2%)	3(9.6%)	0.3
Uveitis	3(9.6%)	0(0)	0.07
HLA B27	17(54.8%)	6(19.3%)	0.04
BASDAI, mean	4.66±1.8	4.98±1.94	0.5
BASFI, mean	4.6±2.3	4.8±2.3	0.7
BASMI, m,ean	3.91±1.94	4.18±2.06	0.4

Results

In total, 31 males were compared with 31 females. Mean age at presentation in males was 30.9±8.6 years and females were 36.8±9.8 years and the difference was statistically significant (p=0.007). The median time difference between symptom onset to the presentation to the hospital was 24 months in males and 12 months in females (p=0.012). Out of 31 males, 27 presented with axial manifestations when compared with only 18 females (p=0.001). Peripheral joint symptoms were present at onset in 13 males and in 26 females (p=0.0001). Looking at other clinical manifestations, 13 males and 13 females had enthesitis at presentation (p=1) and in case of dactylitis 1 versus 3 (p=0.3). Three males had a history of anterior uveitis whereas none of the females had uveitis at presentation (p=0.07). On comparing disease activity and functional indices between males and females, mean BASDAI was 4.66±1.8versus 4.98±1.94 (p=0.5), mean BASFI was 4.6±2.3 versus 4.8±2.3 (p=0.7), mean

BASMI was3.91±1.94 versus 4.18±2.06 (p=0.4). Out of 31 males, 17 were positive for HLA B27 and 6 out of 31 females were positive for HLA B27(p=0.04) as per **Table - 1**.

Among the males, 12 were primary ankylosing spondylitis, 8 were reactive arthritis, 6 were nonradiographicspondyl arthritis, 3 were psoriatic arthritis, and 2 were enteropathic spondyloarthritis. Among the females, 5 were primary ankylosing spondylitis, 12 were psoriatic arthritis, 3 were reactive arthritis, 1 was enteropathic spondyloarthritis, 2 were nonradiographicspondyloarthritis, 8 were undifferentiated spondyloarthritis.

Discussion

This study made an attempt to bring out the gender differences between clinical manifestations and the disease severity at onset. We have combined all the spondyloarthritis into a single cohort and made a comparison. In contrary to the notion that the diagnosis of spondyloarthritis is delayed in females, our study showed that they presented to the clinic earlier than the males [10]. Uddin M, et al. showed that peripheral manifestations predominated in males than in females. We have shown that females presented predominantly with peripheral arthritis. A male preponderance was seen for axial symptoms [11]. Wang R, et al. concluded that peripheral arthritis and dactylitis were seen more in females and enthesitis in males. Our study concluded a similar incidence of enthesitis and dactylitis between males and females [12]. In a meta-analysis by Wright Ka et .al, it was concluded that women score higher in BASDAI than men because of increased peripheral joint involvement but this is not true according to ASDAS [13]. The disease severity as well as the functional index measured by BASFI, metrology index as measured by BASMI was almost similar in both males and females. Tournadre, et al. showed significant HLA B27 positivity in males [14]. Similarly, a significant proportion of males were positive for the genetic marker HLA B27 than females. Primary Ankylosing Spondylitis was the predominant subtype in males whereas psoriatic arthritis was the predominant subtype in females. This is in concordance with the study conducted by Haglund, et al. in Sweden. Late age at presentation, shorter disease duration, predominant peripheral manifestations, the lesser prevalence of HLA B27 are the significant differences observed in females [15].

Conclusion

This is the first systematic epidemiology study of axial SpA. The prevalence estimates according to ASAS criteria are 0.70% for axial SpA and 0.35% for non-radiographic axial SpA, with a proportionally higher prevalence in men than women. Overall, the diagnosis of axial SpA in US rheumatology practices appears to be consistent with ASAS classification criteria. A particular challenge will be to agree on a series of approaches with acceptable (low) risk of bias that could operationalize the present classification criteria (which are developed for use in a (specialized) clinical setting) for use in large epidemiological studies. While a large part of the SpA subtypes in epidemiological studies are as yet classified as ‘undifferentiated SpA’, this diagnosis will likely disappear with the acceptance of the new concepts and classification of axial- and peripheral SpA. The application of these criteria in epidemiological studies requires further consideration. HLA B27 positivity is associated with a male preponderance.

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