



ORIGINAL ARTICLE

## Frequency of extra articular manifestations in ankylosing spondylitis patients presented at independent university hospital Faisalabad.

Zafar Ali Zafar<sup>1</sup>, Abrar Ahmad Wagon<sup>2</sup>, Muhammad Ammad Asghar<sup>3</sup>, Muhammad Badar Bashir<sup>4</sup>, Hafiz Salman Saeed<sup>5</sup>

**Article Citation:** Zafar ZA, Wagon AA, Asghar MA, Bashir MB, Saeed HS. Frequency of extra articular manifestations in ankylosing spondylitis patients presented at independent university hospital Faisalabad. Professional Med J 2022; 29(6):757-763.  
<https://doi.org/10.29309/TPMJ/2022.29.06.6722>

**ABSTRACT... Objective:** To determine the frequency of extra articular manifestations in Ankylosing spondylitis patients at Independent University Hospital, Faisalabad. **Study Design:** Cross-sectional study. **Setting:** Rheumatology Division of Internal Medicine Independent University Hospital, Faisalabad. **Period:** June 2020 to June 2021. **Material & Methods:** Consecutive one hundred and thirty-nine adult patients with baseline Ankylosing Spondylitis fulfilling the Assessment of spondyloarthropathy society criteria at early stage and Modified New York criteria in chronic form of disease, and fulfilling the selection criteria, were selected through Non-Probability Convenient Sampling technique for this study. Chi square test was used to compare the frequency of extra articular manifestations among disease duration, age groups and treatment group. A p-value  $\leq 0.05$  was considered statistically significant. **Results:** In this study, 139 number of patients were selected with confirmed diagnosis of ankylosing spondylitis. Mean age of patients was  $32.60 \pm 8.5$  years with age range of 18 to 50 years. Extra articular manifestations were assessed in all selected patients of ankylosing spondylitis. Enthesitis and dactylitis were found in 8.6% (12) of patients. Uveitis was found in 5% (7) of patients. Similarly, psoriasis was found in 4.3% (6) of patients. Lung fibrosis was found in 3.6% (5) of patients. Inflammatory bowel disease was found in 2.9% (4) of patients. **Conclusion:** Assessment of extraarticular manifestations in AS was very important. Timely intervention with specific therapy decreases morbidity and mortality related to disease.

**Key words:** Ankylosing Spondylitis, Disease Duration, Extra Articular Manifestations.

### INTRODUCTION

Ankylosing spondylitis (AS) is a chronic, autoimmune, inflammatory disease of unknown etiology. It belongs to a group of diseases known as spondyloarthropathy, which includes ankylosing spondylitis, reactive arthritis, psoriatic arthritis, inflammatory bowel disease related arthritis, juvenile idiopathic arthritis, and undifferentiated arthritis. Although they belong to single group, but they are heterogenous in nature and having different clinical presentations as well.<sup>1</sup>

Disease is characterized by inflammatory low back pain and stiffness for more than three months, which is usually relieved by activity but not improved with rest. Later, this disease leads to restricted range of motion at spine and limited chest expansion. Radiologically disease presents

as sacroiliitis either unilateral or bilateral on X-rays and syndesmophytes formation of the spine which is a feature of chronic disease.<sup>2</sup> Usually, disease presents before 45 years of age, more in males and up to 95% are associated with HLA B27 positive. Its prevalence varies between 0.4 to 1.4%.<sup>2,3</sup>

Axial disease spectrum classifies as having ankylosing spondylitis, fulfilling the Modified New York criteria or having non radiographic axial disease in the absence of definite sacroiliitis on plan radiograph which is either called early form of AS or a different form of spondyloarthropathy.<sup>4,5,6</sup>

Most of the time it affects axial joints, importantly sacroiliac joints. But also involves the spine, peripheral joints, and inflammation of enthesium,

1. MBBS, FCPS (MED), FCPS (Rheumatology), Assistant Professor Medicine, Independent University Hospital, Faisalabad.  
2. MBBS, FCPS (MED), FCPS (Rheumatology), Assistant Professor Rheumatology, Chandka Medical College Larkana.  
3. MBBS, FCPS (MED), FCPS (Rheumatology), Senior Registrar Medicine, DHQ Teaching Hospital, Sahiwal.  
4. MBBS, FCPS (Medicine), Professor Medicine, Independent University Hospital, Faisalabad.  
5. MBBS, FCPS (Ortho), FRCS (Glasgow), Associate Professor Orthopedics, Independent University Hospital, Faisalabad.

**Correspondence Address:**

Dr. Zafar Ali Zafar  
Department of Medicine  
Independent University Hospital, Faisalabad.  
drzafar353@gmail.com

**Article received on:** 28/07/2021  
**Accepted for publication:** 11/11/2021

joint capsules, and tendon as well, over all called enthesopathy. Calcification and later ossification of inflammatory enthesopathy is the primary basis of disease called ankylosis.<sup>7</sup> Ankylosing spondylitis not only present with inflammation of joints but also has extra articular features as well. These extra articular features have varied spectrum regarding severity and prevalence. Most common extra articular features are both anterior and posterior uveitis, inflammatory bowel disease, lung fibrosis, cardiac conduction defects and aortic insufficiency, osteoporosis, and skin involvement.<sup>7</sup> A lot of attention has been paid regarding the presence of extra articular manifestations in patients with AS, and many of these EAM especially uveitis, IBD, psoriasis has been included in classification criteria for spondyloarthropathy like assessment of spondyloarthropathy society (ASAS) which usually characterize the disease in early stage. Although these features were not included in Modified New York classification criteria for AS, which usually assesses the disease in chronic form.<sup>8</sup> Also, presence of these EAMs affects the prognosis of disease, treatment decision and quality of life as well.<sup>9,10</sup>

Presence of these EAM have been reported in patients with AS and in broader term spondyloarthropathy. Usually, these EAM reported in long standing disease but broader research and early assessment for spondyloarthropathy, these EAMs precedes in several patients fulfilling criteria either for AS or spondyloarthropathy. Different studies reported 18-58% of peripheral arthritis<sup>11,12,13</sup>, enthesitis was reported in 34% to 74% of AS patients<sup>11,12</sup>, uveitis was reported in 22% to 34% of patients during the course of disease<sup>12,13,14</sup>, IBD was reported in 4%-16% of patients<sup>13,15</sup>, and skin manifestations were noted in 4% to 9% of AS patients.<sup>13,14,15</sup>

Although this disease most importantly has spinal inflammation and structural damage, but some patients have a presentation with extra articular manifestations either concomitant with spinal involvement or present only with extra articular features without spinal structural damage. So, such like cases are usually missed by the

clinicians in early stage and are only documented when there is permanent structural damage. Early assessment and documentation of extra articular manifestations and proper intervention with targeted therapy prevent this permanent structural damage and improves the quality of life and decreases morbidity and mortality as well. Also, it gives insight of the extra articular manifestations with Pakistani prospective and their association with different disease measures like duration, pattern, severity and treatment plans of disease.

### OBJECTIVES

1. To determine the frequency of extra articular manifestations in ankylosing spondylitis patients at independent university hospital Faisalabad.
2. To assess the association between disease duration and extra articular manifestations.

### MATERIAL & METHODS

This cross-sectional study was carried out at Rheumatology division of internal medicine Independent University Hospital Faisalabad, from June 2020 to June 2021. Consecutive one hundred and thirty-nine adult patients with baseline Ankylosing Spondylitis fulfilling the Assessment of spondyloarthropathy society criteria at early stage and Modified New York criteria in chronic form of disease, and fulfilling the selection criteria, were selected through Non-Probability Convenient Sampling technique for this study. This study was approved by the Institutional Review Board of the hospital (IUH/IRB/000029).

Inclusion criteria were all patients of either sex, who have been previously diagnosed or newly diagnosed as case of Ankylosing spondylitis and Age more than 16 years and less than 45 years. Patients with diagnosed cases of Osteoarthritis, also other autoimmune diseases like Systemic Lupus Erythematosus, Systemic Sclerosis, and diagnosed cases of infective or metabolic causes of arthritis were excluded.

A sample size of 139 was estimated by using 95% confidence level, 5% margin of error, with expected

frequency of extra-articular manifestations was 10% among AS patients. Patients were explained about the purpose, risk/benefit of the study and informed consent was taken. Demographic data and history including age, gender, hospital registration number, and disease duration and treatment history and primary investigations like Blood complete with ESR, CRP, X Ray of the sacroiliac joints, X Ray of the lumbar and dorsal spine, MRI of the sacroiliac joints and HLA B-27 in some patients was noted.

All patients were assessed clinically for the sacroiliitis and peripheral joints involvement. Sacroiliitis was assessed as local tenderness at sacroiliac joints and also by Patrick test, Range of motion was assessed by Schober test. Tenderness and swelling of peripheral joints were assessed by bimanual method, Small and large joint involvement, symmetry and Asymmetry of peripheral joints was also noted. All patients were assessed for extra-articular features both clinically and by laboratory tests. Uveitis was assessed by ophthalmologist. Patients with Ankylosing spondylitis were routinely referred to eye specialist for assessment of either clinical or sub-clinical uveitis, which was checked by slit lamp examination. Lung fibrosis was assessed by clinical symptoms of dry cough and shortness of breath. Chest X ray posteroanterior view, lung function tests and high-resolution CT chest later confirmed the presence of lung fibrosis. Inflammatory bowel disease was assessed by clinical symptoms of diarrhea, constipation, abdominal pain and distension, and sometimes tender abdomen. Skin manifestations were commonly noted clinically and later confirmed by dermatologist. Psoriatic skin patches were more common in elderly people with spondylitis. Cardiac involvement was confirmed by echocardiography which showed aortic regurgitation. Enthesopathy and dactylitis was confirmed clinically by tenderness at enthesium and sausage swelling of the finger or toe respectively. Also, few patients showed osteoporosis, confirmed by dual energy X ray absorptiometry, showed score  $> -2.5$ . Disease duration with onset of symptoms of inflammation with pain or stiffness or restricted

joint motion less than 10 years or more than 10 years was also noted.

Data was entered and analyzed on computer using IBM SPSS Statistics version 23.0 software program. Data for age, disease duration, were described by using Mean  $\pm$ SD. Data for gender, extra articular manifestations, investigations were described by using frequency and percentages. Frequency of extra articular manifestations was described by percentage as per given criteria. Chi square test was used to compare the frequency of extra articular manifestations among disease duration, age groups and treatment group. A p-value  $\leq 0.05$  was considered statistically significant.

## RESULTS

In this study, 139 number of patients were selected with confirmed diagnosis of ankylosing spondylitis. Mean age of patients was  $32.60 \pm 8.5$  years with age range of 18 to 50 years. Out of 139 patients, 121 (87.1%) were males and 18 (12.9%) were females as shown in Figure-1. All selected patients were grouped according to their age as shown in Table-I. 52.5% of patient were with age group of 31-45 years. 43.2% of patients were from age group of 15-44 years. Only 4.3% of patients were from age group of more than 45 years.

All selected patients of ankylosing spondylitis were also grouped according to their disease duration as well as shown in Table-II. 54% of patients were from disease duration of less than 10 years and 46% of patients were from disease duration of more than 10 years.

All selected patients were assessed for treatment history as well. 43.2% (60) of diagnosed patients or newly diagnosed cases were not taking treatment as shown in Table-III. 32.4% (45) were taking sulphasalazine as a DMARD along with symptomatic treatment. 10.8% (15) were taking methotrexate as a DMARD therapy. Biologic therapy including inj. etanercept and inj. secukinumab were used only 8.6% (12) of patients.

Extra articular manifestations were assessed in all selected patients of ankylosing spondylitis as shown in Table-IV. 75.5% (105) patients were found to have no extra articular manifestations. Enthesitis and dactylitis were found in 8.6% (12) of patients. Uveitis was found in 5% (7) of patients. Similarly, psoriasis was found in 4.3% (6) of patients. Lung fibrosis was found in 3.6% (5) of patients. Inflammatory bowel disease was found in 2.9% (4) of patients.

Significant association was noted between extra articular features and disease duration and treatment groups when Chi square test was applied as shown in Table-V. It was shown that extra articular features were equally present in groups of patients having disease duration of either less than 10 years or more than 10 years. Similarly, comparatively negligible extra articular features were noted in a group of patients receiving biologic disease modifying anti rheumatic drugs like etanercept or secukinumab as compared to patients taking sulphasalazine or methotrexate or not taking any treatment.

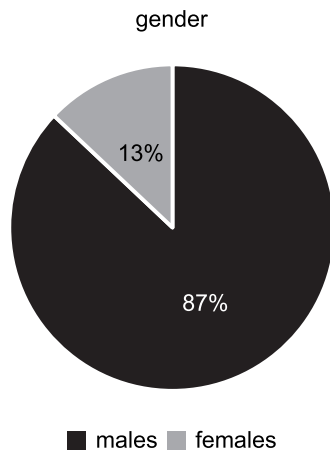


Figure-1.

	Age	Frequency (%)
Valid	15-30	60 (43.2%)
	31-45	73 (52.5%)
	46-60	6 (4.3%)
	Total	139 (100.0%)

Table-I.

Disease Duration		Frequency (%)
Valid	<than 10 year	75 (54.0%)
	>10year	64 (46.0%)
	Total	139 (100.0%)

Table-II

Treatment History		Frequency (%)
Valid	methotrexate	15 (10.8%)
	Sulphasalazine	45 (32.4%)
	Biologics	12 (8.6%)
	Combination	7 (5.0%)
	No treatment	60 (43.2%)
	Total	139 (100.0%)

Table-III

Extra_Articular_Feature		Frequency (%)
Valid	no	105 (75.5%)
	Uveitis	7 (5.0%)
	Lung fibrosis	5 (3.6%)
	Skin psoriasis	6 (4.3%)
	IBD	4 (2.9%)
	Enthesitis, dactylitis	12 (8.6%)
	Total	139 (100.0%)

Table-IV

Variable	Group	Extra Articular Features		P-Value
		Yes	No	
Age	≤ 30 years	14	46	< 0.001
	30 - 45 years	15	58	
	> 45 years	5	1	
Disease Duration	≤ 10 years	17	58	0.005
	> 10 years	17	47	
Treatments	No treatment	8	52	< 0.001
	MTX	9	6	
	Sulphasalazine	15	30	
	Biologics	1	11	
	Other groups	1	6	

Table-V. Group comparison with extra articular features.

**DISCUSSION**

Ankylosing spondylitis and all other forms of spondyloarthropathies are highly prevalent and more disabling group of diseases that initially cause chronic arthritis mostly involving axial spine as well as peripheral joints. Sometimes this disease leads many types of extra-articular manifestations as well.<sup>16,17</sup>

In our study majority of patients are males which comprises almost 87% which is comparable to

another study conducted in Netherland.<sup>15,18</sup>

Our findings on peripheral disease especially enthesitis and dactylitis in consistent with some studies<sup>6,16</sup>, and different findings are noted from other studies.<sup>12,19</sup> A lot of factors have been noted for these different findings. We have studied peripheral disease findings most of the time clinically as assessed in BASDAI score. Also, most patients not report peripheral findings because of the dominance of axial disease. Also, patients with axial disease take the counter medicines for peripheral disease from local physicians so most of time we missing these findings. Studies showing higher percentage of peripheral findings are due to the strict selection criteria and also the availability of musculoskeletal ultrasound and MRI to detect these findings which increases the prevalence of enthesitis and dactylitis.

In our study uveitis was noted in 5% of the cases which are comparable with some studies that showed pooled prevalence of current uveitis of 5.6% and 8.7%.<sup>16,20</sup> But some studies showed prevalence of uveitis range from 21% to 33%.<sup>15,16,21</sup> A lot of factors contribute to this difference in prevalence of uveitis. In our study we selected patients with ankylosing spondylitis and with history of current evidence of uveitis. While few studies have different selection criteria. They selected patients with uveitis and assessed for presence of AS. Also, few studies have done general screening for all selected patients for uveitis and it showed some patients with subclinical uveitis, still not evident clinically, increasing the prevalence of uveitis. Increased duration of disease, more disability and HLA B27 positivity also causes more uveitis.<sup>22</sup>

Skin psoriasis were noted in 4.3% of patients presented with AS. Comparable findings were noted in recent study conducted in China which showed 6.7% psoriasis in AS and some other studies which showed 4-5% prevalence of psoriasis.<sup>23,24,25</sup> Although few studies showed psoriasis prevalence of up to 10%.<sup>15,16,26</sup> This higher prevalence might be due to selection criteria because some patients with psoriasis present with spondyloarthropathy even at age

more than 60 years. Also, it was noted that higher prevalence of psoriasis in European countries as compared to Asian and Middle East countries.<sup>15</sup>

Lung fibrosis and inflammatory bowel disease was found in 3.6% and 2.9% respectively. A recent study<sup>27</sup> done in Sweden showed the prevalence of IBD of 7% which is slightly higher than our study results. Although some studies showed prevalence of IBD up to 34% in ankylosing spondylitis patients. Reason of this higher prevalence is selection of patients which were done all over the country in Swedish study and also massive screening and invasive investigations done in other studies to detect IBD findings. Also, patients with IBD usually not reporting in rheumatology clinic because of priority of gastrointestinal symptoms management and neglecting musculoskeletal part of disease. No patient with amyloidosis, osteoporosis, or any cardiac manifestation was noted in my study.

These extra-articular manifestations were significantly associated with age groups (p value<0.001), disease duration (p-value 0.005) and treatment groups (p-value < 0.00). Longer the disease duration, higher will the systemic inflammation, more the extraarticular manifestations.<sup>9,15,25</sup> Also, people taking regular treatment especially anti-TNF inhibitors like etanercept were the least to have these extraarticular manifestations. A lot of studies have confirmed early diagnosis at the stage of non-radiographic spondyloarthropathy and then regular and proper treatment according to recent guidelines prevent the development of these extra articular manifestations.<sup>28,29</sup>

Our study has certain limitations. This study was cross sectional so it was difficult to generalize the results because of the small sample size. No screening was done to document the extra articular manifestations in its very early form. Similarly histopathological findings of all extraarticular manifestations were not done due its invasiveness and also lack of other departmental support. Association of treatment and extra articular manifestations cannot be generalized because of affordability issues of patients, most

were not treated with specific therapy, so anti-inflammatory response of these drugs not be assessed in all patients. Due to all these factors, more research on a prospective design on a large scale is needed. Also, thorough assessment with histopathological findings is needed to assess the extraarticular manifestations on their very early stage, so timely intervention with proper anti-inflammatory treatment can be done to arrest the disease and extra articular manifestations early so that morbidity and mortality related to disease or extra articular manifestations can be decreased.

## CONCLUSION

Spondyloarthropathy related EAMs are highly prevalent but are often missed during clinical assessment. So proper and careful assessment of these manifestations and timely specific therapy can decrease the morbidity and mortality related to these manifestations.





Copyright© 11 Nov, 2021.

## REFERENCES

- Linden S, Brown M, Kenna T, Maksymowych W, Robinson P editors in **KELLEY & FIRESTEIN'S textbook of rheumatology**.10<sup>th</sup> ed. Philadelphia, PA: Elsevier; 2017:1256-1257.
- Linden S, Valkenburg HA, Cats A. **Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria.** Arthritis Rheum. 1984; 27:361–368.
- Khan MA. **Epidemiology of HLA-B27 and arthritis.** Clin Rheumatol. 1996; 15(Suppl 1):10–12.
- Robinson PC, Wordsworth BP, Reveille JD, Brown M. **Axial spondyloarthritis: A new disease entity, not necessarily early ankylosing spondylitis.** Ann Rheum Dis. 2013; 72:162–4.
- Huerta-Sil G, Casasola-Vargas JC, Londono JD, Rivas-Ruiz R, Chavez J, Pacheco-Tena C, et al. **Low grade radiographic sacroiliitis as prognostic factor in patients with undifferentiated spondyloarthritis fulfilling diagnostic criteria for ankylosing spondylitis throughout follow up.** Ann Rheum Dis. 2006; 65:642–6.
- Ciurea A, Scherer A, Exer P, Bernhard JJ, Dudler J, Beyeler B, et al. **Tumor necrosis factor alpha inhibition in radiographic and nonradiographic axial spondyloarthritis: Results from a large observational cohort.** Arthritis Rheum. 2013; 65:3096–106.
- EM Abdellah, **Extra-articular manifestations of ankylosing spondylitis: Prevalence, characteristics and therapeutic implications.** Eur J Intern Med. 2011 Dec; 22(6):554-60.
- Bengtsson K, Elia HF, Deminger A, Klingberg E, Dahlin M, Exarchou S et al. **Incidence of extra-articular manifestations in ankylosing spondylitis, psoriatic arthritis and undifferentiated spondyloarthritis: Results from a national register-based cohort study.** Rheumatology; 2020; 00:1–10.
- Elewaut D, Matucci-Cerinic M. **Treatment of ankylosing spondylitis and extra-articular manifestations in everyday rheumatology practice.** *Rheumatology (Oxford)* 2009; 48:1029–35.
- Brophy S, Pavy S, Lewis P, et al. **Inflammatory eye, skin, and bowel disease in spondyloarthritis: Genetic, phenotypic, and environmental factors.** *J Rheumatol* 2001; 28:2667–73.
- Ciurea A, Scherer A, Exer P, Bernhard JJ, Dudler J, Beyeler B, et al. **Tumor necrosis factor alpha inhibition in radiographic and nonradiographic axial spondyloarthritis: Results from a large observational cohort.** Arthritis Rheum. 2013; 65:3096–106.
- Vander Cruyssen B, Ribbens C, Boonen A, Mielants H, de Vlam K, Lenaerts J, et al. **The epidemiology of ankylosing spondylitis and the commencement of anti-TNF therapy in daily rheumatology practice.** Ann Rheum Dis. 2007; 66:1072–7.
- Heuft-Dorenbosch L, van Tubergen A, Spoorenberg A, Landewé R, Dougados M, Mielants H, et al. **The influence of peripheral arthritis on disease activity in ankylosing spondylitis patients as measured with the Bath Ankylosing Spondylitis Disease Activity Index.** Arthritis Rheum. 2004; 51:154–9.
- Exarchou S, Redlund-Johnell I, Karlsson M, Mellstrom D, Ohlsson C, Turesson C, et al. **The prevalence of moderate to severe radiographic sacroiliitis and the correlation with health status in elderly Swedish men—the MrOS study.** BMC Musculoskelet Disord. 2013; 14:352.
- Stolwijk C, van Tubergen A, Castillo-Ortiz JD, Boonen A. **Prevalence of extra-articular manifestations in patients with ankylosing spondylitis: A systematic review and meta-analysis.** Ann Rheum Dis. 2015; 74:65–73.
- Janneke JW, Leonieke JM, Désirée VH, Robert L, Dominique LB. **Prevalence of peripheral and extra-articular disease in ankylosing spondylitis versus non-radiographic axial spondyloarthritis: A meta-analysis.** Arthritis Res Ther. 2016; 18(1): 196.

17. Reveille JD, Witter JP, Weisman MH. **Prevalence of axial spondylarthritis in the United States: Estimates from a cross-sectional survey.** *Arthritis Care Res (Hoboken)* 2012; 64:905–10.
18. Suellen NI, Rita NF, André R, Jorge E, Passos P, Germana BE. **Ultrasound of entheses in ankylosing spondylitis patients: The importance of the calcaneal and quadriceps entheses for differentiating patients from healthy individuals.** *Clinics (Sao Paulo)* 2019; 74: e727.
19. Rudwaleit M, Haibel H, Baraliakos X, Listing J, Märker-Hermann E, Zeidler H, et al. **The early disease stage in axial spondylarthritis: Results from the GERman SPondyloarthritis Inception Cohort.** *Arthritis Rheum.* 2009; 60:717–27.
20. Mitulescu TC, Popescu C, Naie A, Predețeanu D, Popescu V, Alexandrescu C, Voinea LM. **Acute anterior uveitis and other extra-articular manifestations of spondyloarthritis.** *J Med Life.* 2015 Jul-Sep; 8(3): 319–325.
21. Zeboulon N, Dougados M, Gossec L. **Prevalence and characteristics of uveitis in the spondyloarthropathies: A systematic literature review.** *Ann Rheum Dis* 2008; 67: 955–959.
22. Rademacher J, Poddubnyy D, Pleyer U. **Uveitis in spondyloarthritis.** *Ther Adv Musculoskelet Dis.* 2020; 12: 1759720X20951733.
23. Siliang M, Xiaojian J, Lidong H, Yiwon W, Yingpei M, Lei W et al. **Characteristics associated with the occurrence and development of acute anterior uveitis, inflammatory bowel disease, and psoriasis in patients with ankylosing spondylitis: Data from the Chinese ankylosing spondylitis prospective imaging cohort.** *Rheumatol Ther* (2021) 8:555–571.
24. Wallis D, Haroon N, Ayearst R, Carty A, Inman RD. **Ankylosing spondylitis and nonradiographic axial spondyloarthritis: Part of a common spectrum or distinct diseases?** *J Rheumatol.* 2013; 40:2038–41.
25. Essers I, Ramiro S, Stolwijk C, Blaauw M, Landewé R, van der Heijde D, et al. **Characteristics associated with the presence and development of extra-articular manifestations in ankylosing spondylitis: 12-year results from OASIS.** *Rheumatology (Oxford).* 2014; 54:633–40.
26. Plunkett A, Marks R. **A review of the epidemiology of psoriasis vulgaris in the community.** *Australas J Dermatol* 1998; 39:225–32.
27. Bengtsson K, Forsblad H, Deminger A, Klingberg E, Dehlin M, Exarchou S et al. **Incidence of extra-articular manifestations in ankylosing spondylitis, psoriatic arthritis and undifferentiated spondyloarthritis: Results from a national register-based cohort study.** *Rheumatology* 2020; 00:1–10.
28. Fragoulis GE, Liava C, Daoussis D, Akriviadis E, Garyfallos A, Dimitroulas T. **Inflammatory bowel diseases and spondyloarthropathies: From pathogenesis to treatment.** *World J Gastroenterol.* 2019 May 14; 25(18): 2162–2176.
29. De Keyser F, Van den Bosch F, Mielants H. **Anti-TNF-alpha therapy in ankylosing spondylitis.** *Cytokine.* 2006; 33:294–298.

### AUTHORSHIP AND CONTRIBUTION DECLARATION

No.	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Zafar Ali Zafar	Introduction, data analysis and discussion writing.	
2	Abrar Ahmad Wagon	Introduction.	
3	Muhammad Ammad Asghar	Review.	
4	Muhammad Badar Bashir	Review.	
5	Hafiz Salman Saeed	Data Collection, Proof reading.	