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Relationship between smoking, clinical, inflammatory, and radiographic parameters in patients with ankylosing spondylitis

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Abstract

Background: Ankylosing spondylitis (AS) is an autoimmune multisystemic disease that attacks the spine, sacroiliacs, and often causes asymmetrical peripheral oligoarthritis. It results from the interaction between the genetic factors mainly Human Leukocyte Antigen B27 (HLA B27) and environmental factors. Current smoking has been reported to be a major risk factor for the incidence and progression of ankylosing spondylitis. So, we aim to explore the relationship between smoking and each of the clinical, inflammatory markers, functional limitation, and radiographic progression in ankylosing spondylitis patients.

Results: Fifty ankylosing spondylitis patients were included in this study. Comparisons of clinical data, radiographic, and inflammatory markers among smokers and nonsmokers revealed that AS current smokers showed a statistically significant decrease in chest expansion, increase in the occiput to wall distance ($p < 0.001$**), higher inflammatory marker, higher disease activity indices (Ankylosing Spondylitis Disease Activity Score, Bath Ankylosing Spondylitis Disease Activity Index), higher Bath Ankylosing Spondylitis functional index, and modified Stoke Ankylosing Spondylitis Spine Score than nonsmokers ($P < 0.001$**). The smoking index was positively correlated with BASFI, ASDAS, (mSASSS) ($r = 0.584$, $p = 0.005$*) and negatively correlated with chest expansion.

Conclusions: Current smoking in ankylosing spondylitis patients is associated with higher disease activity, inflammatory markers, functional disability, and radiological progression. This may add to the disease burden and thus interferes with the personal daily activities, physical mobility, life quality, and the response to TNFi therapy. So, stopping smoking is a mandatory step in controlling the disease activity and having favorable outcome.

Keywords: Ankylosing spondylitis, Smoking, Chest expansion, ESR, CRP, BASDAI, BASFI ASDAS, mSASSS, TNF response

Background

Axial spondyloarthropathies (SPA) are chronic, often progressive, inflammatory disorders of the axial skeleton. The spondyloarthritis prototype is ankylosing spondylitis (AS) [1]. Ankylosing spondylitis patients complain of pain, fatigue, limited spinal motility, functional disability, and impaired psychological well-being [2].

Cigarette smoking plays a dangerous role in developing several diseases. One of these diseases, smoking has participated in the etiology of chronic inflammatory disorders including rheumatoid arthritis [3].

Recent studies have taken up the influence of smoking on spondyloarthritis (SPA). All the previous studies demonstrated there is a complicated association between smoking and ankylosing spondylitis.

Aim of the work

To study the relationship between smoking and each of clinical data, inflammatory markers, and radiographic parameters in patients suffering ankylosing spondylitis

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to examine if smoking carries extraburden to the disease.

Methods

The current study is an observational cross sectional study, including 50 adult ankylosing spondylitis patients diagnosed according to the modified New York criteria [4]. Patients were selected from the outpatient clinic and the inpatients of the Internal Medicine and Rheumatology Department. The study included current smokers, exsmokers (stopped smoking more than 1 year), and nonsmokers ankylosing spondylitis patients with ages > 18 years.

Using PASS 11 program for sample size calculations at setting power 80%, significance level 0.05 and by reviewing the results of studies showed the mean and SD of Schober's test in patients with ankylosing spondylitis in smokers vs nonsmokers were (1.4 ± 1.2 vs 2.5 ± 1 respectively) based on that the sample size needed will be at least 40 patients to be sufficient to achieve study objective.

Exclusion criteria: Other seronegative spondyloarthropathy and associated systemic diseases cardiac, respiratory, other autoimmune diseases (systemic lupus erythematosis, rheumatoid arthritis, scleroderma), and shisha smokers were excluded from the study.

Full history taking including articular, extraarticular disease manifestations, and smoking history were obtained. A quantitative measure for smoking was calculated (one pack years = twenty cigarettes/day for 1 year) age, gender, disease duration, anti-tumor necrosis factor (TNF) medication used at the time of evaluation. All patients provided written consent.

Physical examination, spinal mobility tests (Schober's test, chest expansion, occiput to wall distance), clinical tests of sacroiliac joints (Patrick's (FABER) test, Gaenslen's test, lateral pelvic compression test) were performed.

Disease activity, functional assessment, and radiographic parameters

The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) [5], The Bath Ankylosing Spondylitis functional index (BASFI) [6], Ankylosing Spondylitis Disease Activity Score (ASDAS) [7]. Measuring erythrocyte sedimentation rate (ESR mm/h) and C-reactive protein (CRP mg/dl), and complete blood picture for each patient. Human Leukocytic Antigen B27 (HLA-B27) test was obtained from the patients who essentially performed it for their diagnosis.

Plain radiographs of sacroiliac joints, lumbosacral, and cervical spine including anteroposterior and lateral views were performed. The radiographic damage severity was tested by the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) [8]. Radiographs were scored by an experienced radiologist.

Statistical analysis

Obtained data were analyzed. Quantitative data were illustrated as mean ± standard deviation (SD). Qualitative data were illustrated as frequency and percentage.

The following tests were done: Independent-samples t test of significance. Chi-square (x^2) test of significance. Pearson's correlation coefficient (r) test was used to assess the degree of association between two sets of variables. The p value was considered significant as the following: Probability (P value) ≤ 0.05 was significant, P value ≤ 0.001 was highly significant, P value > 0.05 was considered insignificant.

Ethical consideration

Approval of the study conduction was obtained from the Ethical Committee, the aim of this study was explained to all participants, and confidentiality was assured, written informed consent was obtained.

Results

Fifty Ankylosing Spondylitis patients were included in the study. This study showed that 27 (54%) patients were never smoked, 20 (40%) were current smokers, and 3 (6%) were past smokers. In the study, they were categorized into 2 groups, group I, which included current smokers, and group II, the non-smokers including past and never smokers. The smoking index for current smokers ranged from 1 to 18 years (mean 7.33 ± 5.29). Descriptive data (demographic, clinical, laboratory, and radiographic data) of the patients are shown in Table 1.

Comparisons of clinical, radiographic, and acute phase reactants between group I and group II are demonstrated in Table 2 which shows a statistically significant decrease in chest expansion ($p < 0.001$**) and increase in the occiput to wall distance ($p < 0.001$**) in smokers than non-smokers. Regarding disease activity indices, it demonstrates that smokers had a significantly higher BASDAI ($P < 0.001$**), BASFI ($P < 0.001$**), and ASDAS ($P < 0.001$**) compared with non-smokers which reflects more functional disability and disease progression in smokers AS patients. Additionally, most of the smokers had grade IV sacroiliitis while most of the non-smokers had grade III. Also, there was a highly statistically significant difference between the two groups as regards mSASSS ($p < 0.001$**) which reflects more radiographic progression in smokers. Regarding acute phase reactants ESR ($P = 0.029$*) and CRP ($P < 0.001$**), they were significantly higher in smokers in comparison with non-smokers. As regards uveitis, we found 3 patients only had uveitis. There was an insignificant difference between them.

Table 1 Demographic, clinical, laboratory, and radiographic data of the patients with ankylosing spondylitis (AS) included in the study (n = 50)

Parameters	Total (n = 50)	Group 1 (n = 20)	Group 2 (n = 30)
1-Age (years): range (mean)	20-53 [24. 28 ± 8.30]	24-53 [33.85 ± 7.36]	20-51 [34.57 ± 8.99]
2-Gender: male/female no (%)	39 (78%)/11 (22%)	20 (100%)/0 (0.0%)	19 (63.3%)/11 (36.7%)
3-Family history of AS: +ve/−ve no (%)	6 (12%)/44 (88%)	1 (5%)/19 (95%)	5 (16%)/25 (83%)
4-Disease duration			
Duration of symptoms (years): range (mean)	6-29 [13.24 ± 5.81]	6-29 [13.30 ± 5.97]	6-25 [13.20 ± 5.81]
5-Current medications			
NSAIDS: no (%)	34 (68%)	16 (80%)	18 (60%)
Biologics: no (%)			
Etanercept	39 (78%)	17 (85%)	22 (73.3%)
Adalimumab	7 (14%)	2 (10%)	5 (16.7%)
6-Extra-articular manifestations			
Uveitis: no (%)	3 (6%)	2 (10%)	1 (3%)
7-Spinal mobility			
Patrick's (FABER) test: no (%) Positive, bilateral	50 (100%)	20 (100%)	30 (100%)
Schober's test (cm): range (mean)	1.5-4.5 [2.69 ± 0.84]	1.5-3 [2.70 ± 0.64]	2-4.5 [2.68 ± 0.96]
Chest expansion (cm): range (mean)	2-4 [3.12 ± 0.63]	2-3.5 [2.68 ± 0.41]	2-4 [3.42 ± 0.57]
Occipt to wall distance (cm): range (mean)	0-20 [5.22 ± 6.31]	5-20 [10.90 ± 5.23]	0-12 [1.43 ± 3.50]
8-Disease activity indices			
BASDAI: range (mean)	2.5-5.9 [4.38 ± 1.09]	5-5.9 [5.49 ± 0.36]	2.5-5.5 [3.65 ± 0.72]
BASFI: range (mean)	3.4-6.4 [4.70 ± 0.98]	4.4-6.4 [5.54 ± 0.58]	3.4-6.4 [4.15 ± 0.78]
ASDAS: range (mean)	2.4-4.5 [3.49 ± 0.67]	3.5-4.5 [4.06 ± 0.32]	2.5-4.4 [3.12 ± 0.56]
9-Radiological assessment			
mSASSS: range (mean)	12-72 [43.42 ± 16.63]	40-72 [57.85 ± 9.01]	12-67 [33.80 ± 13.23]
10-Relevant laboratory data			
ESR (mm/h): range (mean)	7-125 [51.32 ± 21.78]++	40-125 [59.45 ± 21.21]	7-100 [45.90 ± 20.76]
CRP (mg/l): range (mean)	4-98 [35.04 ± 20.87]	40-63 [50.90 ± 7.35]	4-98 [24.47 ± 20.76]
HLA-B27: +ve/−ve/not done: no (%)	7 (14%)/3 (6%)/40 (80%)	3 (75%)/1 (25%)	4 (66.7%)/2 (33.3%)
11-Smoking Index for current smokers (pack-year): range (mean)	---	1-18 [7.33 ± 5.29]	---

Quantitative data were expressed as mean ± standard deviation (SD); qualitative data were expressed as frequency and percentage
No number, *AS* ankylosing spondylitis, *NSAID* non-steroidal anti-inflammatory drug, *FABER* flexion abduction external rotation, *Cm* centimeter, *BASDAI* Bath Ankylosing Spondylitis Disease Activity Index, *BASFI* Bath Ankylosing Spondylitis functional index, *ASDAS* Ankylosing Spondylitis Disease Activity Score, *mSASSS* modified Stoke Ankylosing Spondylitis Spine Score, *ESR* erythrocyte sedimentation rate, *CRP* C-reactive protein, *HLAB27* Human leuckocyte Antigen B27, *mm/h* millimeter per hour, *mg/l* milligram/liter, *DMARD* disease-modified antirheumatic drugs

The correlations between smoking index for current smokers (pack-year) and clinical, laboratory, and radiographic variables are shown in Table 3. Pack years were positively correlated with BASFI (r = 0.568, p = 0.007*) (Fig. 1), ASDAS (r = 0.396, P = 0.046*) (Fig. 2), and mSASSS (r = 0.584, p = 0.005*) (Fig. 3) and negatively correlated with chest expansion (r = −0.593, p = 0.005*) (Fig. 4).

Discussion

Ankylosing spondylitis (AS), one of the spondyloarthropathy, is a chronic inflammatory autoimmune disease that mainly affects spine and sacroiliac joints. In the past, before the rising of biologic therapy, it can cause spine fusion [9]. Immune cells and chemical cytokines have been proved to be important in the pathogenesis of AS, especially human leukocyte antigen (HLA)-B27 and the interleukin-23/17 axis [10].

Cigarette smoking is incriminated in the etiology of numerous diseases and took a serious interest worldwide from the current healthcare givers. Also, it has an impact on both innate and adaptive immunity and plays a dual role in dysregulating immunity through either hyperactivation of pathogenic immune responses or weakened defensive immunity [11].

Table 2 Comparison between smokers and non-smokers AS groups regarding demographic and clinical data

Demographic data	Group 1 (n = 20)	Group 2 (n = 30)	t/x^2#	P value
Gender				
Male: no. (%)	20 (100.0%)	19 (63.3%)	9.402#	0.002*
Female: no. (%)	0 (0.0%)	11 (36.7%)		
Age (years): range (mean)	24-53 [33.85 ± 7.36]	20-51 [34.57 ± 8.99]	0.088	0.768
Duration of symptoms (years): range (mean)	6-29 [13.30 ± 5.97]	6-25 [13.20 ± 5.81]	0.003	0.953
Parameters	Smokers (n = 20)	Non smokers (n = 30)	t/x^2#	p value
1. Spinal mobility				
Schober test (cm)	2.70 ± 0.64	2.68 ± 0.96	0.005	0.946
Chest expansion (cm)	2.68 ± 0.41	3.42 ± 0.57	24.989	< 0.001**
Occipt to wall distance (cm)	10.90 ± 5.23	1.43 ± 3.50	58.983	< 0.001**
2. Disease activity indices				
BASDAI	5.49 ± 0.36	3.65 ± 0.72	111.720	< 0.001**
BASFI	5.54 ± 0.58	4.15 ± 0.78	46.203	< 0.001**
ASDAS	4.06 ± 0.32	3.12 ± 0.56	45.972	< 0.001**
3. Radiological assessment				
Sacroilitis grade				
Grade 2	1 (5%)	10 (33.3%)	7.761#	0.021*
Grade 3	9 (45%)	14 (46.7%)		
Grade 4	10 (50%)	6 (20%)		
mSASSS	57.85 ± 9.01	33.80 ± 13.23	50.346	< 0.001**
4. Laboratory data				
ESR (mm/h)	59.45 ± 21.21	45.90 ± 20.76	5.027	0.029*
CRP (mg/l)	50.90 ± 7.35	24.47 ± 20.29	31.035	< 0.001**
3. Extra articular manifestations				
Uveitis	2 (10.0%)	1 (3.3%)	2.405#	0.662
3. Current medications				
NSAIDS	16 (80%)	18 (60%)	2.206#	0.137
DMARDS				
Methotrexate	3 (15%)	2 (6.7%)	0.952#	0.621
Sulfasalazine	1 (5%)	2 (6.7%)		
Biologics				
Adalimumab	2 (10%)	5 (16.7%)	0.965#	0.617
Etanercept	17 (85%)	22 (73.3%)		
Corticosteriods	0 (0.0%)	1 (3.3%)	0.680#	0.409

The P value was considered significant as the following: Probability (P value) P value ≤ 0.05 was considered significant, P value ≤ 0.001 was considered as highly significant, P value > 0.05 was considered insignificant. (*) significant, (**) highly significant

No number, *AS* ankylosing spondylitis, *NSAID* non-steroidal anti-inflammatory drug, *FABER* flexion abduction external rotation, *Cm* centimeter, *BASDAI* Bath Ankylosing Spondylitis Disease Activity Index, *BASFI* Bath Ankylosing Spondylitis functional index, *ASDAS* Ankylosing Spondylitis Disease Activity Score, *mSASSS* modified Stoke Ankylosing Spondylitis Spine Score, *ESR* erythrocyte sedimentation rate, *CRP* C-reactive protein, *HLAB27* Human leuckocyte Antigen B27, *mm/h* millimeter per hour, *mg/l* milligram/liter, *DMARD* disease-modified antirheumatic drugs

And so, there is a complicated association between smoking and spondyloarthropathy [12]. Although some findings are suggesting increased severity of the disease with smoking [13, 14], the mechanism is still unclear [15].

In the present study, we have studied the relationship between smoking and each of the clinical data, inflammatory markers, functional limitation, and radiographic progression in patients with ankylosing spondylitis.

Table 3 Correlation between smoking index for current smokers (pack-year) with other parameters in the AS study groups

Parameters	Smoking index for current smokers (pack-year)	
	r value	*P* value
ESR (mm/h)	−0.181	0.432
CRP (mg/l)	−0.104	0.653
Schober test (cm)	−0.049	0.832
Chest expansion (cm)	−0.593	0.005*
Occipt to wall distance (cm)	0.317	0.161
BASDAI	0.320	0.158
BASFI	0.568	0.007*
ASDAS	0.396	0.046*
mSASSS	0.584	0.005*

Pearson's correlation coefficient (r) test was used to assess the degree of association between two sets of variables
BASDAI Bath Ankylosing Spondylitis Disease Activity Index, *BASFI* Bath Ankylosing Spondylitis functional index, *ASDAS* Ankylosing Spondylitis Disease Activity Score, *mSASSS* modified Stoke Ankylosing Spondylitis Spine Score, *ESR* erythrocyte sedimentation rate, *CRP* C-reactive protein

Regarding the clinical examination, the smokers had highly statistically significant decrease in chest expansion and increase in occiput to wall distance which reflects more disease progression. This was in acceptance with Kaan and Ferda [16], and Averns et al. [17].

Akyol et al. [18] reported that AS decreases and limits the expansion of the chest by affecting costosternal and costovertebral joints, thereby leading to restrictive respiratory distress. Pleuropulmonary tissue was also found to be injured and fibrosis could occur because of inflammatory processes within the lung parenchyma in AS patients. Smoking can also lead to an increase in inflammatory mediators and pain perception due to the effect of nicotine and indirect toxic effects of vasoconstriction or hypoxia [19].

We found insignificant differences between AS patients who currently smoke and AS patients who do not smoke as regards the presence of uveitis (as extra-articular manifestation); three of the studied patients only were having uveitis, and this small number of

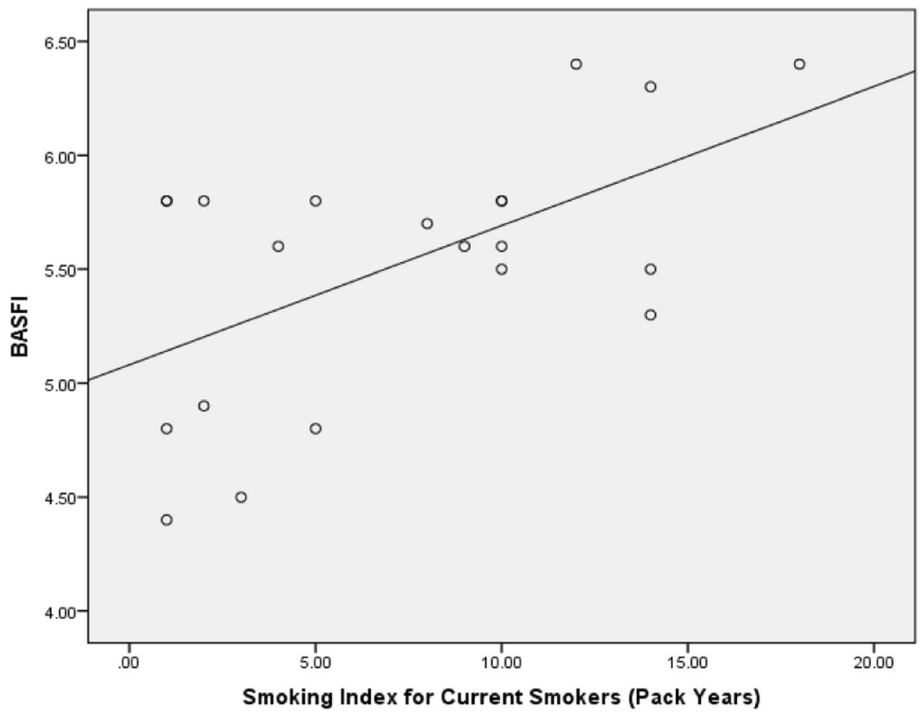

Fig. 1 Correlation between smoking index and BASFI in AS patients. BASFI: Bath Ankylosing Spondylitis functional index

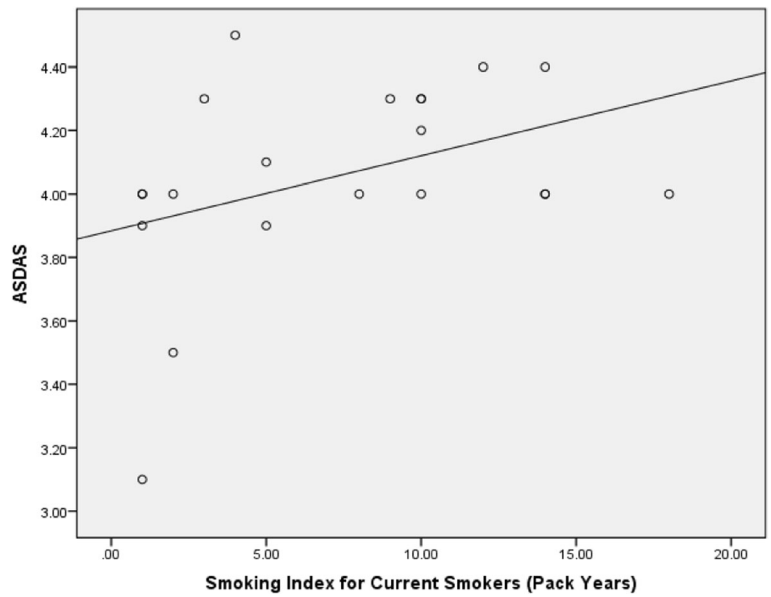

Fig. 2 Correlation between smoking index and ASDAS in AS patients. ASDAS: Ankylosing Spondylitis Disease Activity Score

patients could not reflect the effect of smoking on developing uveitis as extraarticular manifestation of the disease. However, Yeun et al. [20] found that the incidence of new-onset uveitis increased among current smokers compared to never smokers. Also, there are several pathologic mechanisms that may explain the connection between smoking cigarette and uveitis based on long-term exposure to the high concentration of oxidants and polycyclic aromatic hydrocarbons in the serum of cigarette smokers which lead to an increase in the inflammatory mediators [21, 22]. One of those is increasing the transcription of the leukocyte chemoattractant IL-8. Elevated concentrations of IL-8, as observed in the aqueous of the eye in uveitis, act together with IL-6 and TNF-α to promote the migration and activation of macrophages that attack the uvea [23].

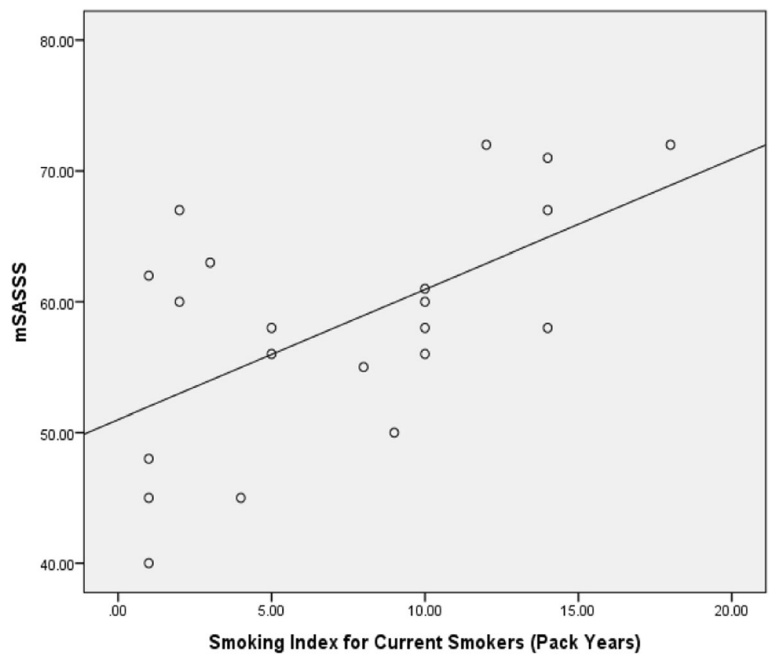

Fig. 3 Correlation between smoking index and mSASS in AS patients. mSASSS: modified Stoke Ankylosing Spondylitis Spine Score

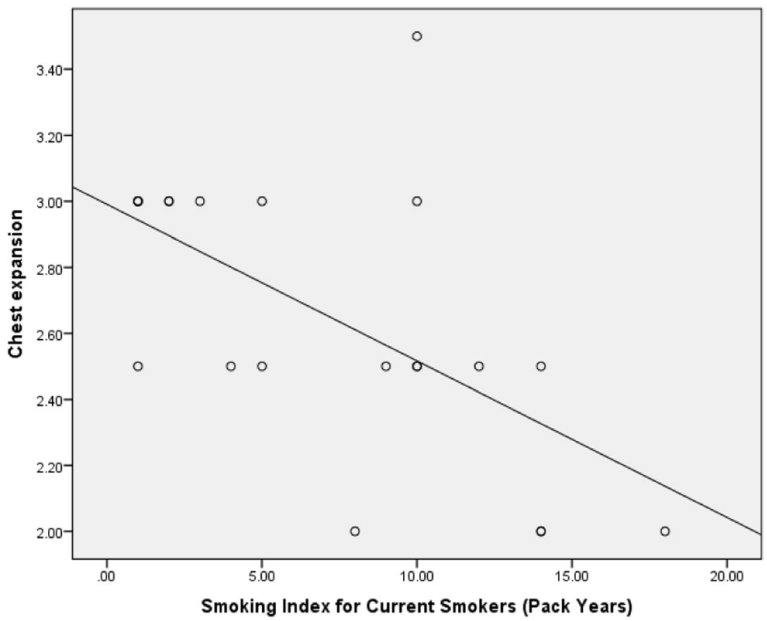

Fig. 4 Correlation between smoking index and chest expansion in AS patients

Regarding laboratory data, the current smoker AS patients had higher mean ESR and highly significant CRP values. This finding is reflecting the presence of higher level of inflammatory markers in smokers AS patients. This was in agreement with Bazzano et al. [24]; Fröhlich et al. [25] who showed that smoking is significantly associated with elevated inflammatory markers especially CRP. Contrary to our results, Klingberg et al. [26] reported no differences in the level of erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) between smoking based groups. ESR and CRP have been used in combination to diagnose and monitor multiple conditions for many years. CRP is somewhat preferred as a serological marker for acute inflammatory disease [27].

As regards disease activity indices, our study showed that AS smoker patients had a higher significant disease activity and functional disability [28]. Dalyan et al. [29], Kaan and Ferda [16], Mattey et al. [30], Chung et al. [14], Fallahi et al. [31], Jones et al. [32], Zhang et al. [33], all suggested similar results. Also, regarding the radiological assessment, we found 50% of AS smoker patients had greater radiographic progression than non-smokers AS patients. Chung et al. [14], Poddubnyy et al. [34], and Sakellariou et al. [35] reported similar findings.

Smoking increases the prevalence of low backache and degenerative diseases of the spine, which may participate in the negative impact of smoking in AS patients [36].

In addition, cigarette smoking was proven to reinforce the manufacturing of numerous pro-inflammatory cytokines such as TNF-α, IL-1, IL-6, IL-8, and GM-CSF (Granulocyte-macrophage colony-stimulating factors), and lower the levels of anti-inflammatory cytokine including IL-10. This inhibitory effect of anti-inflammatory cytokines production is thought to be due to the direct toxic effect of nicotine [37].

Talbot et al. [38] showed that smoking results in aggravation of arthritis and increases the rate of production of Th17 cells in animal models [38]. Th17cells is responsible for regulating the immune response that leads to clearance of extracellular pathogens including bacteria and fungi, and inducing tissue inflammation [38, 39]. IL17 is a main cytokine released fromTh17, which takes critical role in the AS pathogenesis [40]. Subsequently, smoking results in increasing IL-17 which affects bone metabolism by activating the release of matrix metalloproteinases from macrophages and the receptor activator of NF-κB ligand (RANKL) presented by osteoblasts. Furthermore, IL-17 directly affects osteoclasts and activates osteoclastogenesis [40].

Recently, Sakellario et al. [41] demonstrated that smoking enhances the release of the vascular endothelial growth factor (VEGF), which is considered a signaling protein that performs a critical function in angiogenesis. The latter has a role in osteogenesis as well as the incidence of sacroiliitis, enthesitis, and syndysmophytes formation [41].

This may suggest that smoking was related to progressive structural damage in AS because the patients who currently smoke had significantly more syndesmophytes than those who had never smoked [42].

Dulger et al. [43] and Jones et al. [32] showed that smoking cessation improves chest expansion, disease

activity, and life quality; this could be considered as an expected result of decreased systemic inflammation.

Although most of the studied patients received TNF inhibitors (etanercept and adalimumab), the AS smoker patients had very high mean disease activity by ASDAS score in comparison to those in non- smokers. This was similar to a Swiss cohort study which concluded that current AS smokers had worse response rates versus non-smoker AS patients treated with TNFi [44]. Also, they found that current smokers revealed no improvement in disease activity scores (BASDAI and ASDAS scores) upon treatment with TNFi [44].

Demirjian et al. [45] showed that cigarette smoking activates human macrophages and induces the release of TNF-α [45] and increased matrix metalloproteinase levels [36, 46, 47] which may have negative effects and decrease the response to TNFi therapy in AS smoker patients.

In addition, the present study showed a highly statistically significant positive connection between the smoking index and each of BASFI, ASDAS, and mSASSS. A significant negative correlation was also noticed between Smoking Index and chest expansion. This was in agreement with prior studies of Reed et al. [48], Ward et al. [49], and Zhang et al. [33]. All reported that "The greater intensity of smoking is linked with worse outcomes in AS" [33].

Poddubny et al. [50] and Jiang et al. [51] reported that the sequel of smoking on disease activity, functional limitation, development of structural damage in the spine, and the radiographic spinal progression in axSPA is dependent on the intensity of smoking and appears to be caused by upsurge systemic systemic inflammation in smokers.

Finally, regarding the duration of symptoms, there was no significant difference between the smoker and non-smoker AS patients. This was consistent with the results found by Kaut et al. [52] and Gaber et al. [53]. However, Sakellariou et al. [35] found that smoking is positively associated with the duration of inflammatory backache.

Conclusion

Current smoking carries an extraburden on ankylosing spondylitis patients and was associated with higher disease activity, inflammatory markers, functional disability, and radiological progression, and thus interferes with the personal daily activities, physical mobility, quality of life, and the response to TNFi therapy. So, stopping smoking is a mandatory step in controlling the disease activity and having favorable outcome.

Limitation of study

We have only 3 patients who stopped smoking; we need more patients to assess the effect of smoking stoppage in improving disease outcome.

Abbreviations

As: Ankylosing spondylitis; NSAID: Non-steroidal anti-inflammatory drug; FABER: Flexion abduction external rotation; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis functional index; ASDAS: Ankylosing Spondylitis Disease Activity Score; mSASSS: Modified Stoke Ankylosing Spondylitis Spine Score; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; HLAB27: Human leukocyte Antigen B27; GM-CSF: Granulocyte-macrophage colony-stimulating factors; VEGF: Vascular endothelial growth factor; Th: T-helper lymphocyte; IL: Interleukin; RANKL: Receptor activator of NF-κB ligand; Ax SpA: Axial spondyloarthritis; TNFi: Tumor necrotic factor inhibitor

Acknowledgements

Not applicable.

Authors' contributions

HF gave the idea of the research and design of the work. MA was responsible for revision the current research. RH contributed to writing, shared in clinical part of the research at Ain Shams University Hospital (from the rheumatology department and the rheumatology clinic). RH contributed to writing (main role). The authors read and approved the final manuscript.

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Availability of data and materials

The data that support the finding of this study are available at Rasha Mohamad Hassan (the corresponding author) on reasonable request.

Declarations

Ethics approval and consent to participate

Approval of study conduction was obtained from the Research Ethical Committee at the Faculty of Medicine Ain Shams University, No. FWA00001785/MS182. All patients included in this study gave written informed consent to participate in this research.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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