

Clinical-epidemiological aspects in a cohort of ankylosing spondylitis patients

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Abstract

Background. Ankylosing spondylitis (AS) is a disease with onset at a young age, which influences the patient's social life and work capacity.

Aims. The study aims to analyze the epidemiological aspects and clinical characteristics of patients with AS (age of onset, residence, the average duration of the disease, risk factors - smoking, diabetes).

Methods. We conducted a retrospective analysis, descriptive, based on 21 patients diagnosed with AS, hospitalized consecutively, according to the Assessment of SpondyloArthritis international Society (ASAS) criteria, who were evaluated based on personal history and through clinical, biological and imaging evaluation, within the Rheumatology Clinic, Emergency County Clinical Hospital of Craiova, between October 2019 - October 2022.

Results. Following the descriptive analysis of the patients diagnosed with AS, we established certain particular epidemiological and clinical characteristics of the investigated group: statistically highly significant differences regarding the predominance of male patients, and of people from urban areas, average value at the time of diagnosis of 40.48±16.52 years, the average duration of the disease of 6.71±3.22 years, most patients were smokers, and two-thirds of the study participants were overweight.

Conclusions. Our study revealed a low incidence of AS in Referral Center of Craiova, during the investigated period, October 2019 - October 2022. The patient profile resulting from our study with AS was: man, from the urban residence, aged in the fourth decade of life at the time of diagnosis, with moderate disease activity, and having traditional cardiovascular risk factors, smoking or obesity, which may influence disease activity or inflammation.

Keywords: ankylosing spondylitis, human leukocyte antigen B27, inflammatory arthropathy, prevalence.

Introduction

Ankylosing spondylitis (AS) is an autoimmune rheumatic disease with an insidious onset and chronic course. It is part of the spondyloarthritis family which are defined as inflammatory arthropathies, characterized by the presence of the human leukocyte antigen (HLA) B27 (Braun & Sieper, 2007).

AS is a condition that can have an important impact on the patient's quality of life, given the young age of onset and the severe disabling potential, in the absence of specific individualized therapy.

Although the etiopathogenic mechanisms are still incompletely elucidated, the disease is considered to be the result of the interaction between the innate immune system and the adaptive immune system, with the generation of autoantibodies, on a genetically predisposed terrain and under the influence of predisposing environmental factors

(Ranganathan et al., 2027; Sieper & Poddubnyy, 2020).

Following the therapeutic advances in the field of spondyloarthritis, which can have a major impact on the evolution and can stop the progression of joint destruction, when they are applied as early as possible, the need to establish some biomarkers, which can be integrated in a clinical context, can facilitate a correct early diagnosis and can provide insight into the patients' progress and prognosis. Numerous serum markers have been evaluated to assess disease activity, response to treatment, or as predictors of radiological progression. The difficulty lies in the fact that no biomarker can be used individually for the purpose of assessing disease activity or radiological progression, but they must be integrated in a clinical context, in order to establish an algorithm that can help us optimize individualized therapeutic behavior and improve quality the lives of these patients.

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We aimed in this study to analyze the epidemiological aspects and clinical characteristics of patients with AS - age of onset, residence, the average duration of the disease, risk factors - smoking, diabetes -, hospitalized in the Rheumatology Clinic, Emergency County Clinical Hospital of Craiova, between October 2019 - October 2022.

Hypothesis

The foundation of this research started from the finding that no epidemiological studies were conducted in our Reference Center to analyze patients with AS.

Material and methods

For the implementation of the study, permission was requested and obtained from the Academic and Scientific Ethics and Deontology Commission of the University of Medicine and Pharmacy in Craiova (No. 40/18.02.2019). The study strictly followed the General Data Protection and Privacy Regulation (GDPR) and the Declaration of Helsinki 1975/2008.

Research protocol

a) Period and place of the research

This retrospective study analyzed data from patients who were evaluated in the Rheumatology Clinic, Craiova Emergency County Clinical Hospital, between October 2019 and October 2022.

b) Subjects and groups

To establish the epidemiological characteristics of AS, we performed an analysis based on 21 patients diagnosed with AS (the AS group), hospitalized consecutively, according to the Assessment of SpondyloArthritis international Society (ASAS) criteria (Heijde et al., 2016), who were evaluated anamnesticly, as well as through clinical, biological and imaging evaluation.

c) Applied tests

Demographic and clinical data of patients with AS were taken and analyzed from medical documentation (clinical notes). For each patient, the initial assessment included: contact information, demographic information, personal pathological history, clinical manifestations, laboratory tests, disease activity scores, complications (anemia, infections, pulmonary involvement etc.), drug classes used, and the option current therapeutic.

d) Statistical processing

Patients' data obtained from medical documents were managed and processed with Microsoft Excel. Statistical analysis of the data was performed using the GraphPad Prism 5 trial version (San Diego, CA, USA). Normal variables are presented as mean value with standard deviation (SD). According to data distribution the outcomes were compared with Student t-test. For comparison of discrete outcomes we used Fisher's exact test and Chi-squared test. The statistical threshold α was set to 5%, and the value $p < 0.05$ was considered statistically significant.

Results

Following the descriptive analysis of patients diagnosed with AS admitted to the Rheumatology Clinic, of the Emergency County Clinical Hospital of Craiova, between October 2019 and October 2022, we established the following *epidemiological characteristics* in the group of patients with AS:

- Of the 21 patients investigated and diagnosed with AS, male patients predominated (19 patients), values having statistical significance ($p < 0.0001$) (Fig. 1).

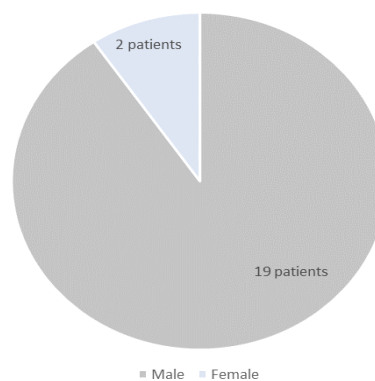


Fig 1 – Distribution of patients by sex.

- Depending on the area of origin, residents from the urban residence constituted the majority of the participants (18 patients), highly statistically significant differences ($p < 0.0001$) (Fig. 2).

- Descriptive data analysis reveals that participants from urban regions demonstrated a higher level of engagement with our survey compared to those from rural areas. Also, the increased level of patients in the urban environment could be explained by the much faster adoption of the westernized lifestyle of the patients in the cities, as well as by the much easier access to health services.

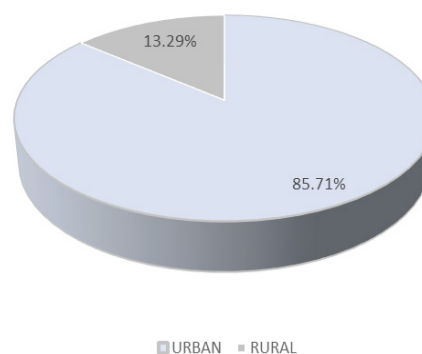


Fig. 2 – Distribution of patients according to the residence.

- Regarding age, the variable had a normal distribution, with an average value at the time of diagnosis of 40.48 ± 16.52 , as shown in Fig. 3.

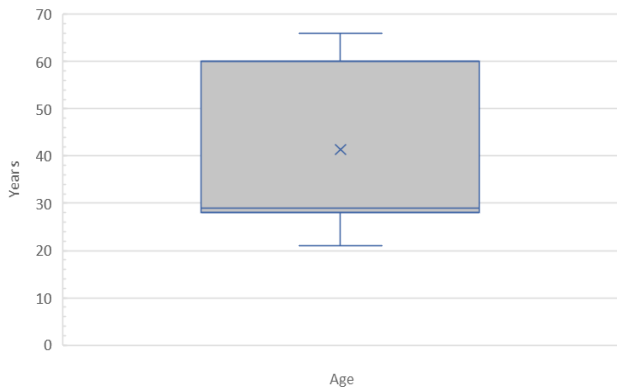


Fig. 3 – Age distribution of the study group.

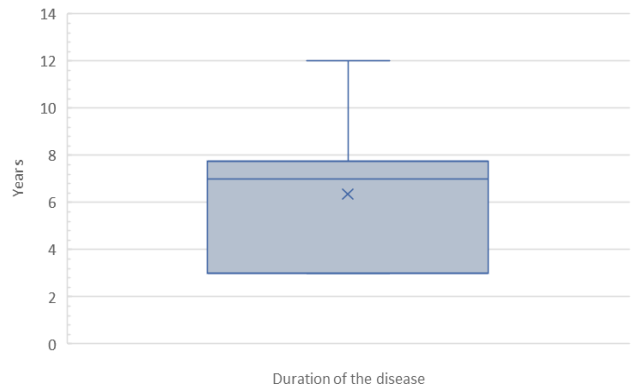


Fig. 6 – Distribution of mean duration of illness in the study group.

- No outliers or older individuals were observed in the AS study groups, female group (Fig. 4) and male group (Fig. 5), respectively, this would make it possible to use the variable for any statistical analysis.

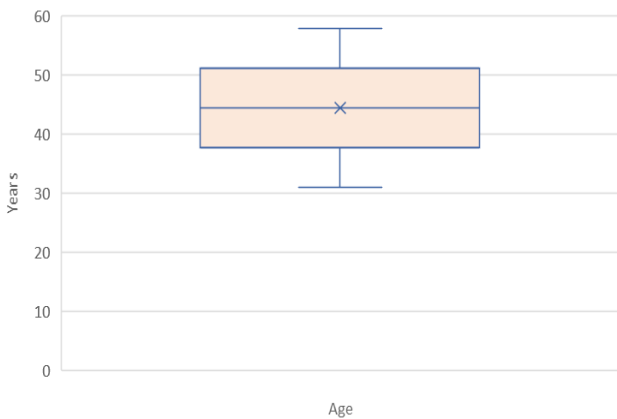


Fig. 4 – Age distribution in the study group - women.

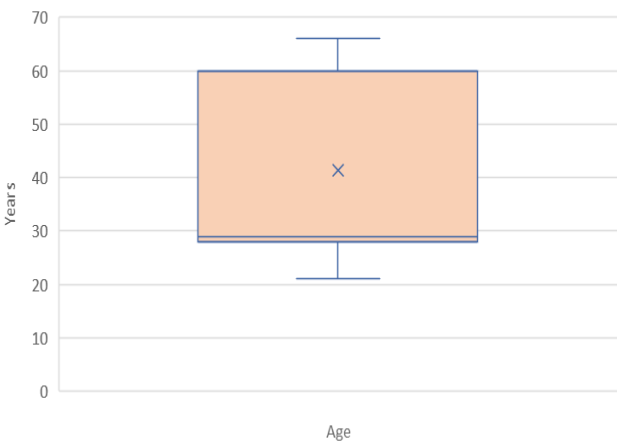


Fig. 5 – Age distribution in the study group - men.

- Regarding the average duration of the disease, it was 6.71 ± 3.22 years (Fig. 6); depending on the SA study groups, in the female group it was 11 ± 1.41 years, respectively in the male group it was 5.50 ± 3.54 .

Regarding the clinical characteristics of patients with AS, we found the following particularities of our study group:

- Depending on the *smoking* risk factor, 11 patients with AS were identified (Fig. 7).

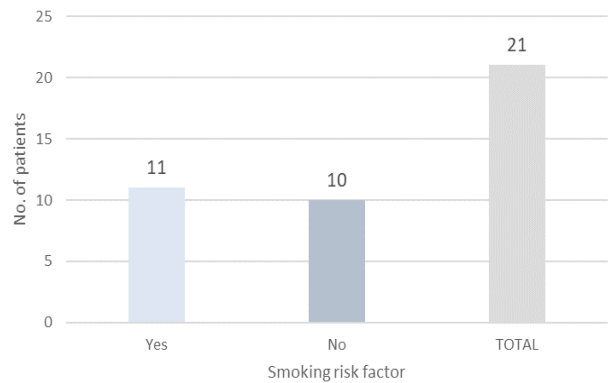


Fig. 7 – Distribution of patients according to smoking.

- *Diabetes* was diagnosed in 8 of the patients with AS (Fig. 8).

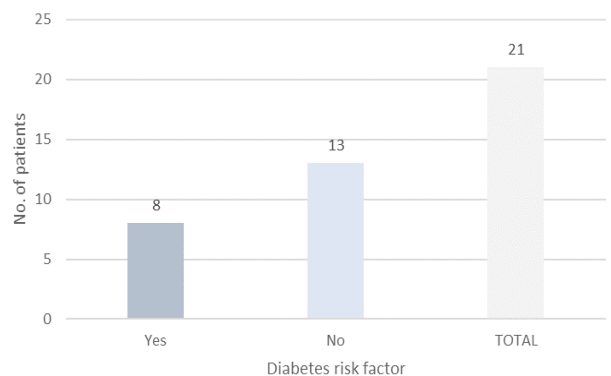


Fig. 8 – Distribution of diabetes in the study group.

- Body mass index (BMI) had an average value of 27.44 ± 6.35 kg/m²sc (Fig. 9). This indicated that two-thirds of the study participants (8 patients, 38.09%) were overweight, while 6 patients (28.57%) had obesity,

traditional cardiovascular risk factors that may influence disease activity or inflammation.

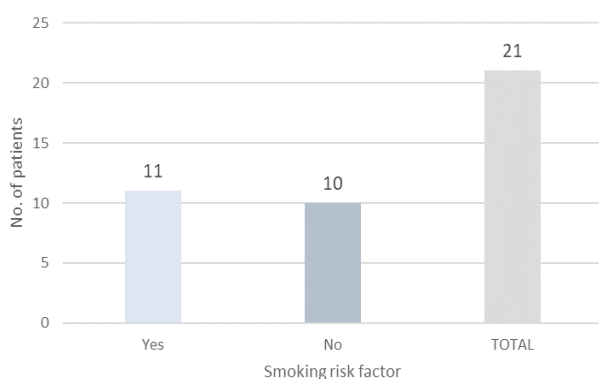


Fig. 9 – Distribution of patients according to BMI.

- Regarding the form of the disease, 15 of the patients had an axial form, and 6 with peripheral damage.

Discussion

Based on our study we outlined the profile of the patient with AS, as derived from the clinical-epidemiological characteristics.

To our knowledge, it is the first epidemiological study performed in our Reference Center Craiova, which provided us with important epidemiological and clinical data characteristic of patients diagnosed with AS.

The incidence of AS in our Center was low, during the investigated period, October 2019 - October 2022, with only 21 patients being diagnosed and hospitalized consecutively. The data are consistent with the few previous observations provided by the studies carried out in Romania, namely in the Iași Reference Center by Țigău et al (Țigău et al., 2008). The authors performed an epidemiological, retrospective, multi-disciplinary study on the prevalence of cases of AS, in Romania and Iași county, in the period 1990-2006. On the sample that included 6,894 cases, a prevalence of 28.86% was recorded in the 35-44 age group with a decreasing trend and 0.07% in the age group 85 years.

A study published by Ionescu et al., 2021 aimed to estimate the cardiovascular risk in young patients with AS. The authors included in the study 70 consecutive patients aged ≤ 50 years (range, 35-50 years) of both sexes, living in rural and urban areas, previously diagnosed with AS and evaluated over a 4-year period (January 2016 - December 2019) at the Constanța County Emergency Hospital.

From the data provided, we find that in our area we recorded a lower prevalence of AS patients compared to the Constanța area.

The prevalence of AS worldwide is estimated to be between 0.1 and 1.4% of the population, but exact figures are difficult to obtain due to the lack of national research results compared to other rheumatic conditions such as rheumatoid arthritis. Furthermore, until now no structured efforts have been made to corroborate data from existing studies on the prevalence of AS (Dean et al., 2014).

It is believed to occur more frequently in those of low socioeconomic status and to result more often in poor

functional status in this population by affecting the spine (Braun et al., 2007; Boonen, 2002; Montacer et al., 2009). Reviews have shown global variation in the background prevalence of the known AS risk allele, human leukocyte antigen B27 (HLA-B27) (Braun et al., 1998; Brewerton et al., 1973) and that 90% of AS patients have this variant, which may likely lead to differences geographic differences in disease prevalence.

Dean et al. conducted a systematic literature review in 2014 to determine the global prevalence and sex ratio of AS by comparing studies for each world region. Thus, they found that the prevalence of AS per 10000 inhabitants was 23.8 in Europe, 16.7 in Asia, 31.9 in North America, 10.2 in Latin America and respectively 7.4 in Africa (based on 36 national surveys). There have been enough studies to estimate the number of cases in Europe and Asia, which have been estimated at 1.30–1.56 million and 4.63–4.98 million, respectively, based on available data (Dean et al., 2014). This study also brought together for the first time the available population data on the gender ratio in SA and the variations between countries, the average gender ratio across all studies was 3.4:1 (male:female) (Dean et al., 2014).

Recent studies have reported that the prevalence of AS ranges from 9 to 30 to 10,000 in the general population, depending on the geographic area, study population or data source, case definition, and ascertainment methods (Exarchou et al., 2015; Barnabe et al., 2017; Dean et al., 2016; Zeng et al., 2015; Julián-Santiago et al., 2016; Curtis et al., 2016; Costantino et al., 2015). Prevalences were higher in selected risk groups. For example, in a Canadian study, the prevalence of AS was three times higher in the First Nations population, a group with a high prevalence of HLA-B27, than in the Non-First Nations population (Barnabe et al., 2017). In a Scottish study, the prevalence was three times higher among patients under the care of rheumatologists compared to those identified in primary care practices (Dean et al., 2016). A US study by Curtis et al. reviewed computerized healthcare data for 13 years from 1996 to 2009; their results found that the prevalence of AS was 22.6 per 10000 (Curtis et al., 2016). In the systematic meta-analysis by Stolwijk et al., the global prevalence of AS ranged from 20.0 per 10000 people in South-East Asia to 161.0 per 10000 in Northern Arctic communities (Stolwijk et al., 2016).

In our study, the age at the time of diagnosis had an average value of 40.48 ± 16.52 , in accordance with the data provided by the study of colleagues from Iasi and higher compared to the study from Constanța where the average age was 32.34 ± 5.34 .

Also, in our study men predominated, a finding also highlighted in the study from Iasi, where the prevalence of men was 84.08%, compared to women (15.91% of the total cases), but also in the one from Constanța where they were diagnosed 54 men and 16 women.

The patients in our study came in most cases from the urban environment, a peculiarity not highlighted in the region of Moldova, where the difference between the areas of residence did not have statistical significance, but was consistent with the results from Constanța where 52 patients from the environment were included in the

study urban and 18 from rural areas. In Iași county, the prevalence of AS had increased values in all 17 years of the study period, higher and often double than those at the national level, and also higher than every county in Moldova and one in western Romania. The authors concluded that the demographic structure, variations and occupational, ecological, economic, educational ones could explain this situation.

The data provided by our study, as well as those of colleagues from Iași and Constanța, underline the fact that the prevalence of AS in Romania in these 3 regions of the country is much lower compared to the data provided by Dean et al. (Dean et al., 2014).

Looking at the age of onset of AS, according to the US Health and Nutrition Examination Survey (NHANES), it is more common in the second and third decades of life (Dillon et al., 2011). It has been estimated that 80% of AS patients present with symptoms before the age of 30 years, while only 5% of those over 45 years of age will have clinical manifestations (Dillon et al., 2011). About 10% to 20% of all patients have the onset of symptoms before the age of 16 years, known as juvenile-onset AS (Feldtkeller et al., 2003).

There may be a delay in diagnosis, occurring several years after the onset of inflammatory rheumatic symptoms (Dillon et al., 2016). Age of onset also correlates with HLA-B27 testing, with those who are positive usually being diagnosed at younger ages. In a study of German and Austrian patients with AS, the age of onset of disease symptoms in HLA-B27-positive individuals was 25 years, while those with a negative test had an average age of 28 years; in addition, there was an 8.5-year delay in diagnoses for those who were HLA-B27-positive, while negative patients had to wait an average of 11.4 years for a diagnosis (Dincer et al., 2008).

A study published by Rezaian MM. et al. had similar results, finding that the age of onset of disease symptoms was 23 years, with a delay in diagnosis of 5.3 years in HLA-B27 positive patients and 9.2 years in those with negative tests (Sampaio-Barros et al., 2001). Of note is that those with inflammatory back pain or a positive family history of AS had a shorter diagnostic delay (Lee et al., 2007).

Women are more likely to report peripheral joint involvement and functional disability, while men have greater axial involvement and severe radiographic damage (Eder et al., 2013). This axial involvement in males was recently studied by Zhu et al. They found that the incidence of AS in men and women is similar in non-radiographic axial spondyloarthritis (nr-axSpA) - which refers to individuals meeting clinical criteria for axSpA without radiological evidence of sacroiliitis (Zhu et al., 2019).

Moreover, in a recent meta-analysis, 2,236 patients with AS and 1,242 with nr-axSpA were evaluated; the results showed that men represented 70.4% of patients with AS and 46.5% of patients with nr-axSpA (de Winter et al., 2016).

Axial involvement in men was also found in our study, 15 of the diagnosed patients had an axial form, and 6 with peripheral involvement.

Conclusions

1. Our study revealed a low incidence of AS in the Referral Center of Craiova, during the investigated period, October 2019 - October 2022.

2. The AS patient profile resulting from our study was: man, from the urban residence, aged in the fourth decade of life at the time of diagnosis, with moderate disease activity, and having traditional cardiovascular risk factors, smoking or obesity, which may influence disease activity or inflammation.

Acknowledgments

The article capitalizes on partial results from the doctoral thesis of Laura-Ioana Crînguș, currently underway at the University of Medicine and Pharmacy of Craiova.

Conflict of interests

None to declare.

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