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# An Epidemiological Study on Ankylosing Spondylitis in Southern Albania

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## ABSTRACT

**Objectives:** To evaluate the incidence and prevalence of ankylosing spondylitis (AS) in southern Albania and to assess the association of various demographic risk factors with the severity of disease. **Material and methods:** This is an observational study with cross-sectional analyses, conducted in the region of Gjirokaster, between 1995 until 2011. The diagnosis of AS was based on the modified New York criteria. Data on population are obtained from the reports of the National Institute of Statistics. **Results:** Between 1995 and 2011, there were 54 patients diagnosed with AS. Of them, 48 subjects were males (88.9%) and 6 subjects females (11.1%). The AS prevalence in adult population ( $\geq 14$  years of age), in December 2010, was 0.061%. The 5-year incidence (2006–2010) in adult population was 0.006%. The mean age at the onset of disease was  $29.7 \pm 8.4$  years. The mean age in 2011 ( $n=50$  subjects) was  $51.6 \pm 12.7$  years. The duration of the disease was  $22.7 \pm 11.2$  years. More than two thirds of the patients (70.3%) were in the advanced radiological stages of the disease. A younger age at the onset of the disease, longer delay in diagnosis, lower educational level and smoking were significant independent factors associated with the advanced forms of the disease. **Conclusion:** In southern Albania, the AS prevalence in 2010 was 0.061% and the 5-year incidence (2006-2010) was 6 new cases per  $10^5$  adults. The incidence and prevalence of AS in Southern Albania are close to the respective regional epidemiological data.

**Key words:** Ankylosing spondylitis, epidemiology, incidence, prevalence, Albania

## 1. INTRODUCTION

Ankylosing spondylitis (AS) is a common rheumatic disease (1). Sacroiliitis is the earliest recognized manifestation of AS, but peripheral joints and extra-articular structures may also be affected (2). The AS prevalence appears to vary among ethnic groups (2) and the incidence mirrors the prevalence of HLA-B27 seropositivity (3). There is a wide geographic variation in the reported prevalence of AS (2), ranging from 0.1% to 6.0% across different populations, with figures for most populations near the lower end of that range (4). Ethnic, racial and geographical factors have been associated with the occurrence and expression of the disease. AS is a chronic disease, that causes considerable pain and disability (5). AS markedly reduces the quality of life for patients and it represents a social burden, as well (6). There are no data on the prevalence and incidence of AS in Albania. The aim of the study was twofold: first, to evaluate the prevalence and incidence of AS in Southern Albania and second, to assess the association of various demographic risk factors with the severity of disease.

## 2. PATIENTS AND METHODS

### Data collection and Region characteristics

This is an observational, cross-sectional study designed to evaluate the prevalence and incidence of AS in adults ( $\geq 14$  years of age) in the region of Gjirokaster, in Southern Albania during the period January 1995 – December 2011. The study included all subjects  $\geq 14$  years of age, who lived in the region and were diagnosed with AS before or

during the study period. Juvenile onset of AS is not included in this study. The Region of Gjirokaster is situated in the southern Albania and regionally is close to Northern Greece. It includes 3 districts, 6 Municipalities, 26 Communes and 273 villages. The region has an area of 2884.26 km<sup>2</sup>. The region has 102549 inhabitants (19982 inhabitants <14 years of age) and 57.7% of the population lives in rural area (National Institute of Statistic, 2010). The climate is Mediterranean. For the entire region, specialized rheumatologic care is provided from the Service of Rheumatology in the Regional Hospital of Gjirokaster. Since the region has no rheumatologic private clinics, all patients were diagnosed, treated and followed by our service. The study cases were gathered from the following sources: polyclinic and hospital of Gjirokaster, health care clinics and family practitioners and regional medical committee for work disability. In all cases, the diagnosis was confirmed by the Rheumatology Service of the University Hospital Center in Tirana (a tertiary university medical center in Albania). Diagnosis was based on the modified New York criteria for AS (7). The diagnostic criteria were fulfilled when a patient presented bilateral sacroiliitis grade  $>2$  or universal sacroiliitis grade  $>3$ , and one of the following: (i) pain in the lower back for at least 3 months; (ii) limited movement of the lumbar spine; and (iii) a reduction in chest opening.

### Clinical parameters

In each identified case with AS, the following data were collected: gender, residence place (village/city), education, profession, age, age at the beginning of the disease, years lived with the disease, disability and disability years, current stage of disease (5 groups), family history,

smoking and alcohol consumption. According to profession patients were divided into two groups: manual labor (worker, miner, farmer, technician, etc.) and non-manual labor (student, teacher, economist, etc.). According to education level, the patients were divided in 3 groups,  $\leq 8$ -year education, high school (8-12 years of education) and university ( $\geq 12$  years of education). Stage of the disease was assessed using radiological criteria: stage 1 (grade II or higher bilateral radiographic sacroiliitis); stage 2 (minor radiographic evidence of spinal involvement in  $< 1$  spinal segment ( $< 3$  vertebrae which equals  $< 15\%$  of the spine); stage 3 (moderate radiographic evidence of spinal involvement in  $< 2$  spinal segments (4–12 vertebrae which equals  $15\text{--}50\%$  of the spine); stage 4 (radiographic evidence of spinal involvement in  $> 2$  spinal segments (13–19 vertebrae which equals  $50\text{--}80\%$  of the spine); stage 5 (widespread [ $> 80\%$  or  $> 20$  vertebrae] fusion of the spine) (8). Disability was defined according to the national criteria of invalidity (9) According to these criteria, preserved mobility with pain is not evaluated as invalidity; reduced mobility but without biological activity of the disease is considered as group I of invalidity. These patients are able to work part time. Limited mobility plus biological activity of the disease is considered as group II of invalidity. These patients are not capable to work.

#### Epidemiologic Parameters

The incidence and prevalence values are calculated as a number of cases for 100 000 inhabitants. Population data are obtained from the National Institute of Statistics. Prevalence was calculated as point prevalence, which is the proportion of the total number of cases in a particular point in time over the total number of the population in that moment. The AS prevalence was calculated in adult population ( $\geq 14$  year of age) at 2 time points: December 2001 and December 2010. Incidence (the number of new cases during a certain time period, over the number of the population at risk at the beginning of the period), was calculated as cumulative incidence for the time period 2006-2010 in adults ( $\geq 14$  years of age).

### 3. STATISTICAL ANALYSIS

The prevalence and incidence were calculated using standard criteria. The distribution of continuous data was tested with the Kolmogorov-Smirnov test. Continuous variables are presented as mean  $\pm$  1 standard deviation when they had a normal distribution, or as median with 25 and 75 percentiles when they had a skewed distribution. The comparison of the data with normal distribution was done using the t-test (for 2 independent groups). Data with skewed distribution were compared using the Mann-Whitney test. Categorical variables (proportions) are presented as absolute numbers and percentages and are compared with the chi square test. The association between risk factors and severity of the disease was tested in multivariable analysis using the multiple logistic regression model. Variables entered into the model were: gender, education, residence, age at the disease diagnosis, disease duration, delay in diagnosis, familial history, smoking, and alcohol consumption. For this analysis, stages—an estimate of disease severity—were grouped into 2 categories: category 1 (stage I + II) and category 2 (stage III-V). The multiple logistic regression model was performed using the Wald backward variable selection method. All analyses were performed using the SPSS statistical package (version 15). A 2-sided P value  $< 0.05$  was considered to indicate statistical significance.

### 4. RESULTS

#### Prevalence and incidence

Overall there were 54 patients with AS who lived in the region of

Gjirokaster, in Southern Albania during years 1995-2011. There were 34 patients in 1995, 44 patients in 2001 and 50 patients living in the region in 2010. Four patients died during this period. The number of adults living in the region in 2001 and 2010 was 84671 and 82567, respectively. The point prevalence of AS in adult population in 2001 was 0.052 %, or 52 cases/ $10^5$  adults. The point prevalence of AS in adult population in 2010 was 0.061% or 61 cases/ $10^5$  adults. The 5-year incidence (2006-2010) of primary AS was 0.006 %, or nearly 6 new cases / $10^5$  adults.

#### Baseline data

During the time period between 1995 and 2011, overall, there were 54 patients with AS living in the region of Gjirokaster. Demographic characteristics of these patients are shown in Table 1.

Variables	Value
Age at 2011 (years)*	51.6 $\pm$ 12.7
Age at the beginning of AS (years)	29.7 $\pm$ 8.4
Gender	
Females,	6(11.1)
Males	48(88.9)
Residence	
City	35 (64.8)
Village	19 (35.2)
Education	
$\leq 8$ years	31 (57.4)
8-12years	19 (35.2)
$> 12$ years	4 (7.4)
Profession as manual labor	47 (87.0)
Invalids	35 (64.8)
Positive Family History	20 (37.0)
Smoking	29 (53.7)
Alcohol consumption	14 (25.9)
Radiographic grading	
Stage I	5 (9.3)
Stage II	11 (20.4)
Stage III	14 (25.9)
Stage IV	18 (33.3)
Stage V	6 (11.1)
Duration of disease (years)	22.7 $\pm$ 11.2
Diagnosis Delay (years)	2.8 $\pm$ 2.4
Disability years (years)**	5.0 [0.0 ; 19.3]
Deceased	4 (7.4)

Table 1. Demographic data. Data are mean  $\pm$  1 standard deviation, median with 25th-75th percentiles or counts (%). \* Four patients who died before 2011 were not included. \*\* The disability years have non-Gaussian distribution, therefore are presented as a median with 25 and 75 percentile (range 0 to 33 years).

The mean age of patients in 2011 was 51.6  $\pm$  12.7 years, ranging from 21 years (1 patient) to 86 years (1 patient). The majority of patients (72%) were  $< 60$  years of age and the 45-55 years age group was most frequent (18% and 26% respectively). The mean age at the AS onset was 29.7 $\pm$ 8.4 years (range 14 to 45 years).

Males comprised 88.9% of the cases and the male/female ratio was 8:1. Nearly two thirds of patients lived in urban areas (64.8%). The majority of patients belonged to the group with lower level of education (57.4%) and had professions qualified as manual labor (87.0%). More than half of the cases smoked (53.7%) and slightly more than one fourths of them used alcohol (25.9%). Familial history for AS was present in 37% of the patients and nearly two thirds of patients were invalids. Overall, the disease duration was 22.7 $\pm$ 11.2 years.

Males had a longer duration of the disease (24.1 years), compared to females (11.8 years,  $P=0.008$ ). The distribution of years with disease is shown in Figure 1.

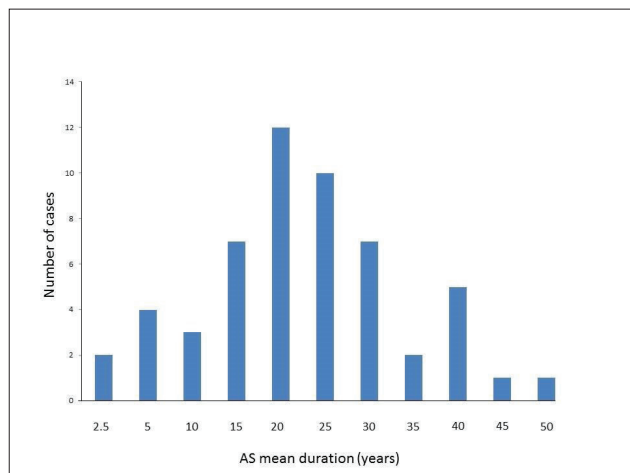


Figure 1. Distribution of the patients according to the disease duration.

Four patients (7.4%) died during the study period. Causes of death were: acute renal failure (1 patient, 41 years of age), chronic renal failure (1 patient, 70 years of age), myocardial infarction (2 patients, 71 and 73 years of age).

Patients belonged to all 5 radiologic stages. Demographic data according to AS stage are shown in Table 2. About two thirds of the patients (70.3%) were in the advanced radiological stages (>15% with diffuse spinal involvement; stages III, IV and V). Overall, patients in the advanced stages of AS had a younger age at the onset of AS, a longer duration of the disease, had more disability years, had longer delay in diagnosis, were more often males, had a lower educational level and smoked and consumed alcohol more frequently compared to patients in lower stages of the disease (Table 2).

Variables	Stages I-II		Stages III-V		P
	Nr.	Value*	Nr.	Value	
Age in 2011 (yrs.)	15	49.7±15.7	35	52.4±11.3	0.486
Age at AS onset (yrs.)	16	33.1±8.4	38	28.3±8.1	0.050
Duration of AS (yrs.)	16	17.8±11.4	38	24.8±10.6	0.034
Disability years**	16	0.0 [0.0; 0.0]	38	8.0 [2.25-20.75]	<0.001
Diagnosis delay (yrs.)	16	1.6±1.3	38	3.3±2.6	0.021
Gender	16		38		0.002
Female	5	31.3%	1	2.6%	
Male	11	68.7%	37	97.4%	
Residence	16		38		0.101
Rural	3	18.7%	16	42.1%	
Urban	13	81.3%	22	57.9%	
Education	16		38		0.004
≤8 years	6	37.5%	25	65.8%	
8-12 years	6	37.5%	13	34.2%	
>12 years	4	25%	0	0.0%	
Manual labor	12/16	75%	35/38	92.1%	0.087
Smoking	3/16	18.8%	26/38	68.4%	0.001
Alcohol consumption	1/16	6.3%	13/38	34.2%	0.029
Familial history	3/16	18.8%	17/38	44.7%	0.071

Table 2. Demographic data according to radiologic stages. \*Data are mean ± 1 standard deviation, median [25th-75th percentiles] or counts (%). \*\*The disability years have non-gaussian distribution; therefore they are presented as median [25th-75th percentiles].

Males (odds ratio [OR] = 16.81 confidence interval [CI] [1.77 to 159.58]  $P=0.0139$ ) and smokers (OR=9.39 [2.25 to 39.22],  $P=0.0021$ ) showed a greater risk for achieving advanced stages of disease.

### The results of the multivariate analysis

The multiple logistic regression model (see methods for variables we adjusted for) was used to identify the independent correlates of the severity of disease (stages). The model identified the following variables as independent correlates of AS stage: age at the AS onset, diagnosis delay, education and smoking. The beta coefficients, direction of the association and p-values of the associations are shown in Table 3.

Variables	Beta coefficient [95%CI]	P value
Age at the onset of disease	0.866 [0.760–0.987]	0.031
Delay in the diagnosis	1.741 [1.009–3.003]	0.046
Education level	0.159 [0.032–0.799]	0.026
Smoking status	7.208 [1.110–46.812]	0.039

Table 3. Independent correlates of the AS stages. CI = Confidence Interval

## 5. DISCUSSION

The main findings of this study are as follows: 1) AS has a prevalence of 0.061% (61 cases in  $10^5$  adults) in 2010 and a 5-year incidence of 0.006% (6 new cases per  $10^5$  adults) during the period 2006-2010 in southern Albania. 2) AS is more prevalent in males than in females with a male to female ratio of 8:1. 3) Factors associated with increased risk for advanced stages of the disease were early age at the AS onset, longer delay in diagnosis, lower educational level and smoking.

AS is a rheumatic disease that is encountered throughout the world, yet its prevalence shows substantial differences across ethnic groups (10), depending on regional, genetic and environmental factors (4). Studies in Caucasian populations (11) from Norway (12), Netherlands (13), Island (14), Germany (1), Greece (15, 16, 17), Turkey (18, 19), Japan (20), and USA (21), suggest the existence of geographical differences in the prevalence of the disease. In general, the AS incidence and prevalence reflect the frequency of Human Leukocyte Antigen (HLA) – B27 in the population (3, 22). This may explain the virtual absence of the disease in South Africa, the low frequency in Japan and Greece, higher levels in Norway compared with other European countries and highest levels among populations living in subarctic regions of Euroasia and North America (23). Dietetic factors such as fish oil consumption in mediterranean diets and mild climatic factors, exposure to the sun and the ultraviolet radiation, may protect against the disease. These factors differ among Mediterranean countries, USA and Northern Europe and may explain, at least, in part, regional differences in the AS frequency. However, the exact role of these factors remains unclear (15). The AS prevalence was reported to be 0.14% among Turkish university students (19), 0.49% in the Ismir region in Turkey (18) and 29.5 cases per  $10^5$  adults (>16 years) in the Ioannina region, in Northwestern Greece (15). The findings of our study showed that the AS prevalence in Southern Albania is lower than in Northern Europe and America and it approximates the AS prevalence in Turkey and Northwestern Greece.

In this study we found a male-to-female ratio of AS of 8:1. The gender differences in population-based studies of AS differ considerably. Thus, the male-to-female ratio has been reported to be 5.6:1 in Turkey (24), 4.7:1 in Northwestern Greece (15), 4:1 in central Greece (17), 5.4:1 in Japan studies (19), 2.3:1 in Finnish studies (25), and 8.1:1 in Korean population (26). Clinical studies in patients with AS have also suggested the existence of male predominance and significant gender differences among various racial and ethnic groups (15). Other studies have suggested that males with AS develop more often functional disability than females (27). By finding a higher risk of functional disability among males, our study concurs with this investigation.

In our study, the age at the onset of the disease was 29.7 years and

the highest frequency was found in the 25 to 35-year age group. Age at the onset of the disease was identified as a significant independent correlate of the severity of AS. AS usually begins in late adolescence or early in the adult age; onset after 45 years is unusual (26). It has been reported that age at the onset of AS has prognostic significance (28) and younger age is associated with a poorer prognosis (29).

Several studies have investigated the influence of socio-economic status and lifestyle factors on the outcomes of the disease (28). Patients with lower educational and socio-economic groups (30) and those with more physical occupation have been reported to have a poorer prognosis (31). Cigarette smoking has been associated with poor long term outcome in patients with AS (32, 33). Chung et al. showed that smoking was associated with an earlier beginning of spinal pain and a higher activity of the disease. It also has been reported that smokers with AS had more physical disability and more advanced radiological damage (34). In our study, more than two thirds of patients were in advanced radiological stages of the disease and these patients had a lower educational level and more likely to be handcraft workers. Of note, our study identified the smoking status and lower education level as significant independent correlates of increased risk for developing advanced stages of the disease.

We recognize some limitations of present study. The focus of the study was AS with the onset in adult age. Consequently, cases with the disease onset in the subjects <14 years of age (juvenile onset of AS) (2) were not included. Due to the lack of information on age structure of the population, the prevalence in specific age-groups was not assessed. Finally we have no data on the frequency of HLA B-27 in our population or our patients. However, in most adult patients, AS can be diagnosed using clinical criteria without HLA-B27 information (35). Moreover, diagnostic criteria for AS are nearly the same, irrespective of information on HLA-B27 (7, 23).

## 6. CONCLUSION

In conclusion, the present study showed that AS had a prevalence of 0.061% (in 2010) and a 5-year incidence of 0.006%. The AS was more prevalent in males than in females. A younger age at the onset of the disease, longer delay in diagnosis, lower educational level and smoking were significant independent factors for advanced forms of the disease. The incidence and prevalence of AS in Southern Albania are close to the respective regional epidemiological data.

**CONFLICT OF INTEREST: NONE DECLARED.**

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