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Epidemiological features and treatment regimen for sarcoidosis of respiratory organs in 2011-2015 in subcarpathian region

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Abstract

This research work is devoted to the study of morbidity and prevalence of sarcoidosis of respiratory organs in Ivano-Frankivsk region (Western Ukraine). The structure of patients was analyzed according to their sex, age group, disease status, blood group, extrathoracic manifestations of the disease and comorbidities. The quality of patients' treatment was evaluated for its compliance with modern standards. The study of the structure of sarcoidosis makes it possible to gain better understanding of the etiological and pathogenetic factors affecting the development of the disease, and thus increase the effectiveness of its treatment.

Keywords: sarcoidosis, epidemiology, treatment.

Introduction

Among various pathologies of the respiratory organs, interstitial diseases continue to attract researchers' attention due to the constant increase in their morbidity rates (about 20% of all lung diseases are related to interstitial processes), diagnosis and treatment problems. Progressive fibrosis of the pulmonary interstitium leads to respiratory failure and pulmonary hypertension with the formation of chronic cor pulmonale and disability^[5].

Interstitial lung disease (ILD) belongs to a heterogeneous group of diseases, often of unknown etiology, characterized by progressive lung deficiency with the presence of inflammatory and sclerotic changes in the structure of pulmonary interstitium^[4].

Currently, sarcoidosis is one of the most common interstitial lung diseases of unspecified origin. For example, in Belgium this pathology accounts for 27% of all ILD cases, in Greece – 34.1%, and 33.7% in Italy^[12].

Numerous epidemiological findings suggest that climatic factor is one of the most distinguished factors in the epidemiology of sarcoidosis^[13]. It is known that this pathology is most widespread in geographic areas with moderate and frigid climate. Consequently, the highest prevalence rates of the disease are observed in Nordic countries and Scandinavian Peninsula (10.1 cases per 100 thousand people in Denmark; 11.4 – in Finland; 15.4 – in Norway and 24.0 – in Sweden)^[6].

Some of the lowest morbidity rates are recorded in the countries of Southern Europe, Eastern Asia and Latin America: 1.37 per 100 thousand people in Spain; 1.01 – in Japan and 0.56 – in Singapore^[12, 14].

The research works performed by Havrysiuk V.K. and his co-authors showed that the lowest morbidity (1.1 per 100 thousand people) and prevalence (4.6 per 100 thousand people) rates in Ukraine were recorded in Crimea, while the lowest rates were observed in Zhytomyr region (morbidity – 2.62 cases per 100 thousand people, prevalence – 7.9 cases per 100 thousand people)^[1,2].

According to literature data, high incidence and more severe course of the disease are observed among dark-skinned population, so in London the disease incidence among Afro-Americans is 12 times higher than among Caucasians^[9, 10]. Dark-skinned US Navy soldiers have 10-17 times higher disease incidence rates as compared to Caucasian ones^[7].

Sarcoidosis occurs more often among women (55-65%). Patients aged from 20 to 49 predominate. The peak disease incidence rate among male population is 20-39 years, and among female-population – 40-60 years.

Analysis of up-to-date foreign and home scientific literature shows that sarcoidosis of intrathoracic localization is predominant worldwide. However, in 30% -50% of cases

extrapulmonary manifestations of the disease are evident, among them the most common are: sarcoidosis of the skin, eyes, liver, spleen, central nervous system.

Numerous epidemiological studies show that chronic forms of sarcoidosis are prevalent in the world. Thus, in Poland patients with Lofgren's syndrome make up only 9% of cases, in Ukraine – 8.3%, in the Balkans – 24%. On the other hand, in Spain and Portugal, the countries with the lowest incidence rate in Europe, almost 50% of patients are diagnosed with an acute form of the disease [3, 8].

Sarcoidosis of respiratory organs occurs in all age, racial and ethnic groups, and the polymorphism of clinical manifestations is closely related to climatic, geographical, gender and occupational factors. In view of this, the current study of the epidemiology of sarcoidosis still remains relevant.

Materials and methods

Statistical data were obtained by processing hospital and

ambulatory medical records of patients from Ivano-Frankivsk regional phthysio-pulmonary centre during the period from 2011 to 2015. The investigation involved male and female patients aged from 18 years, whose diagnosis of sarcoidosis was confirmed either histologically or by means of helical computed tomography of thoracic organs. The patients were divided into groups according to different parameters: district of the region, sex, age, radiologic stage of disease, bad habits, comorbide pathologies and others. The results of the investigation were processed by means of mathematical calculations and Microsoft Office Excel programme.

Results of the investigation

In order to study the structure of patients with sarcoidosis in Ivano-Frankivsk region we have processed 450 hospital records for the period of 2011 - 2015. Totally 278 patients (over 18 years of age) diagnosed with sarcoidosis underwent treatment in Ivano-Frankivsk regional phthysio-pulmonary centre.

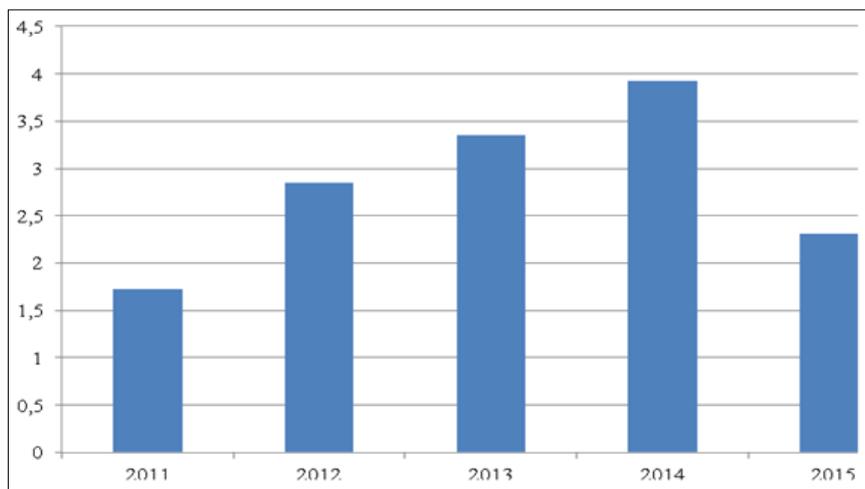


Fig 1: The incidence of sarcoidosis of respiratory organs in Ivano-Frankivsk region (per 100 thousand people)

On average, the incidence rate was 2.83cases per 100 thousand people and showed certain tendency to increase from 1.73 in 2011 to 3.92 cases per 100 thousand people in 2014. The dynamics of disease incidence is shown in Figure 1. The prevalence rate of sarcoidosis in Ivano-Frankivsk region is significantly higher as compared to other regions of Ukraine. The number of patients with active form of sarcoidosis ranged from 4.27 to 5.50 cases per 100 thousand

people (see Figure 2), and averagely it made up 4.97 cases per 100 thousand people within 5 years.

Totally, 278 patients were diagnosed with sarcoidosis for the 5-year period. Therefore, it can be assumed that the prevalence of sarcoidosis in different phases of its activity is 20.14 cases per 100 thousand people that is 2.54 times higher than the maximal rate in Ukraine (7.9 cases per 100 thousand people).

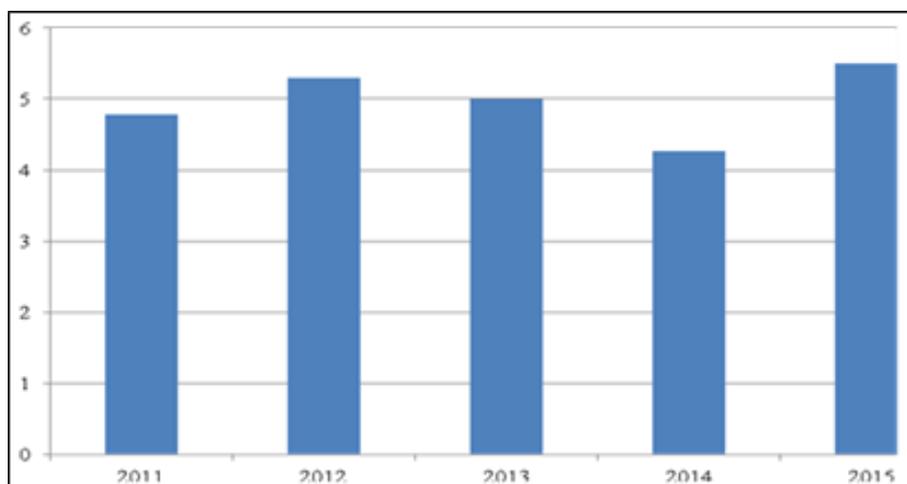


Fig 2: Prevalence of active sarcoidosis of respiratory organs in Ivano-Frankivsk region (cases per 100 thousand people)

The detailed analysis of the indices recorded in different districts of the region made it possible to establish that the highest morbidity rate was recorded in Kalush (7.03 cases per 100 thousand people) and Kolomyia (6.87 cases per 100 thousand people) regions, while the lowest indices were noticed in Sniatyn (0.42 cases per 100 thousand people) and Halych (0.38 cases per 100 thousand people) ones.

The highest prevalence rates of active sarcoidosis in the districts of the region were recorded in Kalush and Kolomyia districts – 9.80 and 10.00 cases per 100 thousand people, while the lowest rates were recorded in – Sniatyn and Tlumach districts – 0.86 and 1.33 per 100 thousand people.

Kalush and Kolomyia districts are known for their chemical, oil-and-gas and machine-building industries. According to the data provided by the Department of Environmental Protection of the region, these districts are considered to be the areas of increased anthropogenic load, because high contents of harmful substances, like nitrogen dioxide, carbon monoxide, formaldehyde are annually found in the air, and significantly exceed the level of allowable concentrations [10]. The average morbidity rate in these districts makes up 6.95 cases per 100 thousand people, that is 2.45 time higher than the average incidence rate in the region ($p < 0.05$).

As evidenced by the data of research literature, wood dust is one of the most common etiological non-infectious factors of sarcoidosis, as wood-working industry is widely developed in Precarpathia. There are about 40 large and average, and 300 small enterprises in the region, most of which are concentrated in Nadvirna, Rozhniativ, Kosiv and Verkhovyna districts. The average morbidity rate here made up 2.73 cases per 100 thousand people, that is somewhat below the average rate recorded in the region, with considerable prevalence of male cases, who are actually involved in the wood-working industry.

While evaluating the climatic factors which are considered as the leading cause of the disease development, we have determined that the average morbidity rate was recorded in the northern part of the region (Rohatyn, Halych and Kalush districts) and averagely made up 3.10 cases per 100 thousand people, and in the southern part (Sniatyn, Kosiv and Verkhovyna districts) this rate was 2.05 cases per 100 thousand people. In the northern regions this rate was 1.51 times higher ($p < 0.05$), that meets the tendency in Ukraine and abroad. It is a well-known fact, that the sarcoidosis morbidity rate is the lowest in African and Asian countries, while in Nordic countries this rate is the highest [3, 22]. According to the research data of Havrysiuk V.K., the lowest incidence (1.1 per 100 thousand people) rates in Ukraine were noticed in Crimea, and the highest rates were marked in Zhytomyr region (2.62 cases per 100 thousand people) [3, 4, 6, 7].

In most cases sarcoidosis was diagnosed with the help of helical computed tomography of thoracic organs (85.26%) and only in 41 patients (14.74%) the diagnosis was confirmed histologically.

148 women (53.23%) and 130 men (46.77%) were diagnosed with sarcoidosis. Disease prevalence among female population is compliant with literature reports [3, 4].

The morbidity rate of female population increases within the ages from 18 to 40 years and rapidly decreases after 49. The peak incidence in male population is from 20 to 29 years of age and decreases by the age of 60 years.

As Table 1 shows, the pathology is rare in the elderly and at the age of 18-20 years, there are only single case records of sarcoidosis.

Table 1: Distribution of patients with sarcoidosis according to the age groups (Ivano-Frankivsk region)

Age	Women		Men	
	Absolute	%	Absolute	%
18-20 years old	1	0.35	4	1.43
20-29 years old	21	7.55	49	17.62
30-39 years old	32	11.51	30	10.79
40-49 years old	47	16.9	22	7.91
50-59 years old	36	12.94	20	7.19
60 years old and older	13	4.67	3	1.07

Acute form of disease (Lofgren’s syndrome) was diagnosed only in 15.82% of cases (44 patients), and in 84.18% of cases (234 patients), the disease ran a chronic course. The largest number of patients with acute form of the disease – 56.81% of cases, was recorded in Kalush (15 cases) and Kolomyia (10 cases).

82.6% of patients were non-smokers and have never smoked before, therefore, no relation between smoking and the incidence of sarcoidosis was revealed [11].

Table 2 shows the distribution of patients according to the radiological stages of the disease. Stage III sarcoidosis was rarely diagnosed – only 10.79% of cases (30 patients), while patients with stage II of the disease were the most common – 56.10% of cases (156 patients). Damage to the pulmonary parenchyma was revealed in more than 80% of cases.

Table 2: Distribution of patients with sarcoidosis according to the stage of disease in Ivano-Frankivsk region

Stage	Women		Men	
	Absolute	%	Absolute	%
I	27	9.71	25	8.99
II	84	30.21	72	25.89
III	14	5.03	16	5.76
IV	23	8.28	17	6.13

In addition, we have studied the distribution of patients with sarcoidosis according to their blood groups (ABO system) and Rhesus factor. The obtained results are presented in Table 3.

Table 3: Distribution of patients with sarcoidosis according to the blood groups (ABO system) in Ivano-Frankivsk region

Blood Group	Number of patients	
	Absolute	%
I	74	26.61
II	125	44.96
III	57	20.50
IV	22	7.91

Regarding the Rh factor: 243 patients (87.41%) – were Rh positive, and 35 (12.59%) patients were Rhesus negative. Pulmonary insufficiency was diagnosed in 91 patients (32.73%), and sarcoidosis was considered to be its main cause in 64 patients (70.32%).

Extra-pulmonary manifestations of sarcoidosis were diagnosed in 31 patients (among them – 18 men (58.06%) and 13 women (41.94%)), which made up 11.15% of the total number of patients. Damage to the peripheral lymphatic nodes was most commonly diagnosed – 29 cases (93.54% of patients). No cases of sarcoidosis of the nervous and urinary systems were detected. The structure of extra-pulmonary manifestations of sarcoidosis is given in Table 4.

Table 4: Occurrence of extra-pulmonary manifestations in patients with sarcoidosis (Ivano-Frankivsk region)

Localization of the lesion	Occurrence (number of cases)	
	Absolute	%
Peripheral lymphatic nodes	29	93.54
Spleen	6	19.35
Eyes	4	12.90
Skin	3	9.67
Liver	3	9.67
Heart	1	3.22
Salivary glands	1	3.22
Joints	1	3.22
Pleura	2	6.45

One of the most important stages of our retrospective study was the investigation of comorbide pathologies in patients with sarcoidosis. 93 patients (33.45%) were diagnosed with obesity of varying degrees. Most of these patients (69-75.82%) have not yet received treatment with systemic corticosteroids.

Figure 6 shows the distribution of comorbide pathologies. It may be noted that the most common pathologies involve the cardiovascular system (coronary heart disease, hypertension) and respiratory diseases (chronic bronchitis, COPD).

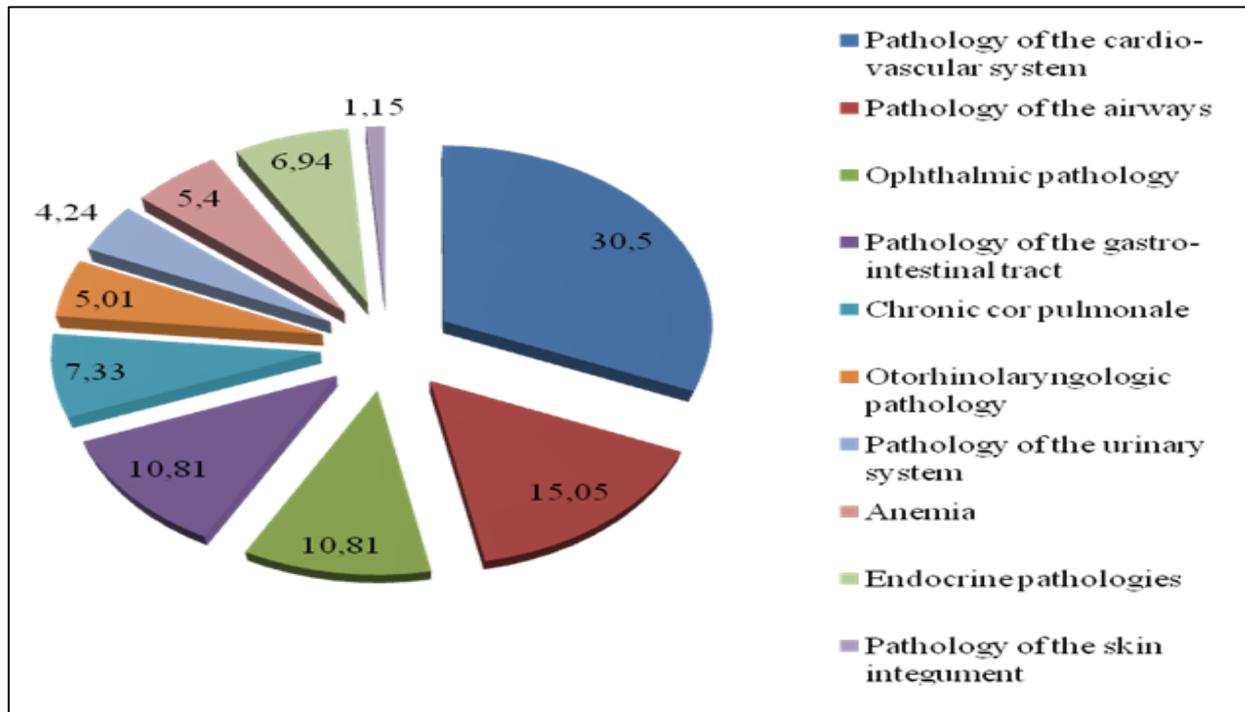


Fig 3: The structure of comorbide pathologies in patients with sarcoidosis in Ivano-Frankivsk region

It should be noted that these indices reflect the situation only among officially registered patients.

The quality of patients' treatment was evaluated for its compliance with modern standards.

Treatment assignment criteria involved:

1. All stages of sarcoidosis with extrathoracic manifestations – damage to the heart, central nervous system, eyes, and hypercalcaemia.
2. Stage II sarcoidosis with clinical manifestations (cough, shortness of breath, chest pain, and decreased physical activity) and/or moderate dysfunction of external respiration.
3. Stage III sarcoidosis.

Doses and regimens of glucocorticoid therapy.

In most patients –78%, dosage and treatment regimens were in line with modern standards. The initial dose of methylprednisolone was 0.4 mg/kg of body weight, and by the end of the 3rd month, the dose was reduced to 0.2 mg/kg and the effectiveness of treatment was evaluated. In case of improvement of clinicoradiological indices the dose was gradually reduced to 0.1 mg/kg up to the end of the sixth month, during the next 6 months the dose remained unchanged.

The daily dose of the drug was divided into 2 intakes – 2/3 of the daily dose in the morning, and 1/3 of the daily dose by noon.

Glucocorticoid (GC) therapy was combined with potassium medications, and in the absence of hypercalcaemia – with calcium medications.

Hydroxychloroquine was administered as a monotherapy in 2% of patients, and in 11% – in combination with glucocorticosteroids. The drug was prescribed at the dose of 200 mg twice a day for 3-6 months (depending on the regression rate), followed by 200 mg once a day by 1 year.

Pentoxifylline was administered in combination with glucocorticoids in case of insufficient effect of GC-therapy. It is administered in daily dose of 1200 mg by infusion or per os.

Conclusions

1. The incidence of sarcoidosis in Ivano-Frankivsk region exceeds the maximal rate in Ukraine and makes up 2.83 cases per 100 thousand people, and the prevalence rate in Precarpathia comprises 20.14 cases per 100 thousand people.
2. In the northern districts of the region, the morbidity rate is 1.10 times higher than the average in the region, and is 1.51 times higher than in the southern parts of Precarpathia.
3. In assessing the gender and age patterns of the prevalence of sarcoidosis, it was revealed that women are more

likely to suffer from this disease – 53.23%, and the peak of the disease incidence is between 40-49. In men, this pathology most often develops between 20-29. Single case reports of sarcoidosis were revealed in individuals under 20 or over 60 years of age.

4. Extra-pulmonary manifestations of sarcoidosis were more commonly diagnosed in men – 93.54% of all disease cases. Damage to the peripheral lymphatic nodes were the most common – 93.54%, while the cases of heart, joint, salivary glands damage were less common.
5. The most common comorbide pathologies involved cardio-vascular (coronary heart disease, hypertension) and respiratory disorders (chronic bronchitis, COPD). Pulmonary insufficiency was diagnosed in 91 patients (32.73%), and sarcoidosis was considered to be its main cause in 64 patients (70.32%).
6. Systemic corticosteroids, namely methylprednisolone, still remains a "gold standard" in the treatment of patients with sarcoidosis of the respiratory organs.

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