Epidemiology of Sarcoidosis in the Precarpathian region of Ukraine

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Abstract: Despite considerable advances in modern medicine, it must be admitted that sarcoidosis is still a disease with unknown etiology, hardly predictable clinical course and, as a result, it is characterized by a variety of diagnostic and therapeutic approaches to patient management. We have studied the morbidity and prevalence rates of sarcoidosis of respiratory organs in Precarpathian region for a 5-year period on the basis of information provided by district and city pulmonologists, phthisiologists and general practitioners for the period of 2011-2015. The incidence of sarcoidosis in Precarpathian region is on average 2.8 new cases per 100 thousand adults per year, which exceeds the corresponding indices not only in the southern (1.1 per 100 thousand adults), but also in the northern (2.6 per 100 thousand) regions of Ukraine. The prevalence of active sarcoidosis reaches 5.0 cases per 100,000 people; the disease incidence in the north of the region is 1.5 times higher as compared with the southern regions. In the territories with increased man-made load the mortality rate is 2.5 times higher than the average index registered in the region, while the prevalence rate is 1.9 times higher, correspondingly. Summing up the results of the study it may be concluded that sarcoidosis has long ceased to be a rare disease and the morbidity and prevalence rates of this ailment depend on geographical and environmental factors.

Keywords: sarcoidosis, epidemiology, prevalence, morbidity.

I. INTRODUCTION

Health level of the population is an important indicant of social and economic state of the society. The quality of health depends on various exogenous factors: natural, ecologal hygiene, industrial, as well as on the living standards of a particular country. Despite the significant achievements in modern medicine, the diagnosis and treatment of respiratory sarcoidosis, as well as the peculiarities of the disease course in various occupational and age groups still remains among the unresolved issues.

Sarcoidosis is a systemic inflammatory disease of unknown nature characterized by multi-system manifestations with a certain frequency of involvement of various organs and activation of T-cells at the site of granulomatous inflammation with the release of various chemokines and cytokines, including tumor necrosis factor (TNF-alpha).

The climatic factor is regarded as one of the most important in the epidemiology of sarcoidosis. It has been established that this pathology is most common in geographic areas with temperate and cold climates. Thus, according to the National Register, in Sweden the prevalence rate of sarcoidosis is about 160 cases per 100 thousand people, while the morbidity rate is 11.4 cases per 100 thousand people, with the highest indices registered in the northern regions of the country [1]. The summarized data registered in Denmark, Finland and Norway show that the morbidity rate in the age group of 18-20 years was 57 cases per 100 thousand people, and the average index among all age groups ranged between 14-15 cases per 100 thousand people [2], [3].

Women are more often diagnosed with sarcoidosis (6.3 cases per 100 thousand people) than men (5.9 cases per 100 thousand people). In view of the results of patients' management in Minnesota (USA) from 1946 to 2013, the researchers have registered the increase in the age-related morbidity rate among women, thus, in 1950, the peak of the morbidity rate was observed between 40-59 years, and in 2010 – 50-69 years. Similar situation was observed among men: in 1950, the peak morbidity rate was registered at the age range of 30-49 years, and in 2010 this rate increased to 40-59 years [4]-[7].

The morbidity rate varies widely across the world between 0.2 and 64 cases per 100,000 people and has a clear tendency to increase, for example, international consensus papers show that the number of patients with sarcoidosis in the world increases by 2% annually [8], [9]. It should be noted that the morbidity rate of sarcoidosis is considerably higher among the coloured population as compared to Caucasians, and ranges between 35-80 cases per 100 thousand people [10]. The examination of US Navy military men during the period from 1958 to 1969 revealed that the morbidity rate among Afro-Americans was 10-17 times higher than among the Caucasians. The re-evaluation of morbidity rates registered in 2001 showed that this rate was about 24.9 cases per 100 thousand people among Afro-Americans, while the corresponding rate among the Caucasians was 3.5 per100 thousand people [11]. The indices of sarcoidosis incidence significantly vary throughout the world and make up averagely 1-40 cases per 100 thousand people [12].
The highest prevalence rates are recorded in the Nordic countries and the Scandinavian peninsula. Thus, in Sweden, a national patient register has been established. It includes all hospital admissions of patients with sarcoidosis from 1964 to 2013 and ambulatory treatment for the period of 2001-2013. The prevalence rate was 160 cases per 100 thousand people. The morbidity rate ranged about 11.4 cases per 100 thousand people, with the highest indices registered in the northern regions of the country. The peak incidence rate among male population was 30-50 years, and among women – 50-60 years [1].

Detailed analysis of the prevalence and morbidity rates was carried out in Switzerland on the basis of outpatient and inpatient records during the period of 2002-2005. 2,925 (0.05%) patients out of 5,590,962 were hospitalized with the diagnosis of sarcoidosis. The average age of male patients was – (52 ± 15) years, and that of female – (58 ± 17) years. 899 cases (31%) were newly diagnosed, and the average age was (45 ± 15) years. The morbidity rate in this period was 7 cases per 100 thousand people. Total prevalence rate made up 121 cases per 100 thousand people, the prevalence rate of active form of sarcoidosis was 44 cases per 100 thousand people, while the number of patients requiring hospitalization was 16 cases per 100 thousand people. The highest prevalence rates were registered among the workers of metallurgical industry, air services and agricultural industry [1]. Epidemiological studies conducted in the submountain regions of the Alps in Switzerland showed that the sarcoidosis morbidity rate in this area was (7 cases per 100 thousand people) considerably higher as compared to the corresponding indices recorded in the neighboring countries, which, according to the authors, may be associated with climate peculiarities in the submountain regions, as well as the influence of certain products of agricultural production [13].

Sarcoidosis is rare in China, India, Australia, New Zealand and the countries of Eastern Asia and South America [14].

US scientists showed clear relationship of the sarcoidosis prevalence rates depending on the patient’s sex, race, and occupation. The morbidity rate of male population ranges from 2.5-7.6 cases per 100,000 people among Caucasians as compared to 13.2-81.8 cases per 100,000 Afro-Americans [15]. The sarcoidosis prevalence rate among fire-fighters was 222 cases per 100 thousand people, while among alerting medical personnel this rate was 35 cases per 100 thousand people. [16]. In Detroit (USA) in 1990-1994, the highest prevalence rate was recorded among black women [11].

Annually more than 700 new cases of sarcoidosis are registered in Ukraine, and the number of patients with an active form of disease exceeds 2500 cases. Approximately 5-7% of cases assume continuous relapsing nature and proceed to generalized pneumosclerosis, which results in severe respiratory failure [17].

Comparative study of the morbidity and prevalence rates of respiratory sarcoidosis in the southern and northern regions of Ukraine, based on the data of patients’ presentations and the results of prophylactic X-ray examination in 2011, showed that: the morbidity rate registered in the south of Ukraine was 1.08 cases per 100 thousand adults, and the prevalence rate was 4.59 cases per 100 thousand people. In the northern part of Ukraine, the morbidity rate (2.62 cases per 100 thousand people) exceeded the corresponding rate in the southern region by 2.4 times. The prevalence rate (7.86 cases per 100 thousand people) was 1.7 times higher than in the south of the country. Taking into account that the climatic factor is the key one in the development of sarcoidosis the conclusion can be made that the morbidity rate in Ukraine ranges from 1.1 to 2.6 cases per 100 thousand people (Fig. 1), and the prevalence rate is from 4.6 to 7.9 cases per 100 thousand people [17].

The study of hospital and ambulatory records of 1,776 patients in 2008-2012, showed that women are dominant in the structure of patients (56.5%). Men (43.5%) are more likely to be diagnosed with sarcoidosis at the age from 20 to 39 years, and among women the peak incidence is recorded in later years – from 40 to 59. Cases of childhood sarcoidosis have not been registered, while among adolescents aged 14-17 years, 9 cases – 0.5% were recorded among the total number of examined patients. Low morbidity rates were also observed among people aged 18-20 years and people over 60 years of age [18].

The profile of patients with sarcoidosis was also evaluated according to the severity of disease course and by radiological stages. Acute form of respiratory sarcoidosis (Löfgren syndrome) was observed in 8.3% of patients, and its chronic form – in 91.7% of cases. Considering the X-ray pattern the distribution of patients was the following: stage I (bilateral hilar lymphadenopathy) – 41.6%; stage II (bilateral hilar lymphadenopathy with lung infiltration) – 43.7%; stage III (lung infiltration only) – 9.9%; stage IV (pulmonary fibrosis) – 4.8%. It should be noted that pulmonary parenchyma was affected in practically 60% of patients (II-IV stage of the disease), which is the key to the development of gas exchange processes abnormalities [18].

The analysis of treatment outcomes showed that the highest rate of unsatisfactory results was observed among patients with stage III of the disease. This may be associated with delayed administration of specific therapy, improper diagnosis of disseminated tuberculosis, compliance of the quality of therapy with modern standards [18].

The findings of retrospective study showed that the mortality rate in the eastern part of Ukraine was 7 cases per 100 thousand people in 2010, and the prevalence rate was 20 cases per 100 thousand people. The number of female patients prevailed – 64%. Their age range was from 22 to 70 years, most of them (94%) were under 50 years of age. 30% of patients were not employed, 86% of patients never smoked, 8% of patients gave up smoking 5-6 years prior to disease onset. In 1/3 of patients, pathologic changes were detected during periodic health examination. In 32% of patients, the disease proceeded asymptomatic, in 48% of patients the disease onset was gradual, and in 20% – acute (all of them were diagnosed with Löfgren syndrome). The main complaints were cough (20% of patients) and dyspnea (in 56% of patients). Obesity of varying degrees was observed in 30% of patients. Among extrapulmonary manifestations, lesions of peripheral lymph nodes (12% of patients) were prevalent; sarcoid skin lesions were observed in 8% of patients in the form of papules, plaques, hypodermic nodules [19].
Kharkiv National Medical University conducted the examination of workers of machine-building enterprises, who have constant contact with industrial dust and aerosols, and they were referred to special facilities suspected of occupational disease. The diagnosis of sarcoidosis was confirmed in 17 patients, in 8 of them the disease developed on the background of silicosis. The scientists evidenced the need to study the extrapulmonary manifestations of sarcoidosis in order to differentiate it from pneumoconiosis [20].

The aim of the research is to study the morbidity, prevalence rate and formation of sarcoidosis of respiratory organs in Precarpathian region for a 5-year period.

II. MATERIALS AND METHODS

The aim of the research is to study the morbidity, prevalence rate and formation of sarcoidosis of respiratory organs in Precarpathian region for a 5-year period.

In order to achieve the stated aim and to solve the assigned tasks of the research work, we have studied the morbidity and prevalence rates of sarcoidosis of respiratory organs in Precarpathian region for a 5-year period on the basis of information provided by district and city pulmonologists, phthisiologists and general practitioners for the period of 2011-2015.

Most of the patients of Precarpathian region were diagnosed with sarcoidosis on the basis of spiral computed tomography of the chest (85.3%) and only 41 cases (14.7%) were histologically confirmed. Such structure in the issue of diagnostic verification of the diagnosis may be explained by the fact that currently the possibilities of multi-slice computed tomography in the morphological diagnosis of respiratory pathological changes have considerably increased, and this is the reason for reducing indications for surgical biopsy of the lungs and mediastinal lymph nodes.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments, and the study was approved by the Committee on Bioethics Questions of Regional Centre of Phthisiology and Pulmonology, Ivano-Frankivsk on 17.11.2017 (Protocol No. 11.02/17).

III. RESULTS AND DISCUSSION

Totally, for the 5-year period, we have diagnosed 278 cases, therefore we can assume that the prevalence rate of sarcoidosis in various phases of its activity is 20.1 cases per 100 thousand people and is 2.5 times higher than the peak value registered in Ukraine (7.9 cases per 100 thousand people). The climatic factor is considered to be the leading one in the development of sarcoidosis, its prevalence and morbidity rates. Significant differences in the rates of morbidity and prevalence of sarcoidosis in the northern and southern regions of one country are observed in Ireland and Denmark – countries that are significantly smaller in their area than Ukraine [21]. Detailed analysis of the indices recorded in different districts of the region made it possible to prove the influence of geographic factor on the disease epidemiology: thus, in the northern part of the region the average index of the morbidity rate was 3.1 cases per 100 thousand people, and in the southern part this index made up 2.1 cases per 100 thousand people. Thuswise, it may be noticed that this index is 1.5 times higher in the northern regions that is common with the general tendency observed both in Ukraine and in the world. In fact, the morbidity rates are the lowest in Africa and Asia, while the highest rates were recorded in Scandinavian countries and these data is closely common to the findings obtained by Ukrainian scientists [17]. Thus, in Ukraine the lowest indices were recorded in the south of the country (1.1 cases per 100 thousand people), and the lowest indices were observed in the north (2.6 cases per 100 thousand people) [17].
Since sarcoidosis most often affects the lungs, skin and eyes, most studies of the disease cause were focused on the search for airborne pathogenic agents. The results of the early studies established the relationship between the disease development and the influence of inorganic particles, insecticides, molds, heavy metals, formaldehyde, phenol resins [17], [21]. The analysis of occupational factors showed high morbidity rates among the workers of metal-processing industry. There are two districts in Preparpathian Ukraine 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. The average morbidity rate in these districts is 7.0 cases per 100 thousand inhabitants, that is 2.5 times higher than the average index recorded in the region and, in our opinion, it confirms the influence of industrial factors on the epidemiology of respiratory sarcoidosis [17].

As evidenced by the data of research literature, wood dust is one of the most common etiological non-infectious factors of sarcoidosis [17]. Wood-working industry is widely developed in mountain regions of Preparpathia: there are about 40 large and average, and 300 small enterprises in the region. However, the average morbidity rate here made up 2.7 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.

Published data show, that women are more commonly diagnosed with sarcoidosis as compared to idiopathic pulmonary fibrosis [6]. According to the results of patients’ observation conducted in Minnesota (USA) between 1946 to 2013, the researchers noted the increase in age-related peak morbidity rates among women, thus, in 1950, the peak rate accounted for 40-59 years, and in 2010 – 50-69 years. Similar pattern was observed among men: in 1950, the peak morbidity rate was at the age of 30-49 years, and in 2010 this index increased to 40-59 years. At the same time, the ratio between female and male diagnosed with sarcoidosis was 1.13:1, which shows the prevalence of female cases and is compliant with other literature reports.

Foreign studies show that the most common comorbid pathologies of sarcoidosis were: diseases of the circulatory system, chronic bronchitis, diabetes mellitus, thyroid gland disorders and damage to the gastrointestinal tract [2], [7]-[9]. It may be noted that the most common comorbid conditions observed in investigated patients were diseases of the circulatory system (ischemic heart disease, hypertensive disease) – 30.5%, and respiratory organs (chronic bronchitis, COPD) – 15.1%, while the pathologies of ENT organs (5.0%), urinary system (4.2%) and skin (1.2%) were comparatively rare [17].

The research works [6] and [7], show that people with excessive body weight are at higher risk to develop sarcoidosis of respiratory organs as compared to smokers. We have also diagnosed various levels of obesity in 93 patients (33.5%). Most of these patients (69,0-75,8%) have not been treated with systemic corticosteroids yet. The significant proportion of the surveyed – 17.4%, both men and women, were either smokers or former smokers. Therefore, the relationship between tobacco smoking and sarcoidosis may be ruled out, which coincides with the opinion of many other authors.

**IV. CONCLUSION**

In Ukraine, prevalence of sarcoidosis was studied in the northern, southern and eastern regions, but there were no data on the epidemiological features of this pathology in the western regions of the state. Our studies have confirmed the influence of geographic and environmental factors on the epidemiology of respiratory sarcoidosis. Thus, the morbidity rate of sarcoidosis in Preparpathian region exceeded the corresponding index not only in the southern (1,1 cases per 100 thousand people), but also in the northern (2.6 cases per 100 thousand people) regions of Ukraine, which may be explained by the prevalence of sarcoidosis among the inhabitants of mountainous areas and on territories with increased man-caused load.

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**REFERENCES**


