

EPIDEMIOLOGICAL, CLINICAL – EVOLUTIONARY AND DIAGNOSTIC ASPECTS OF HODGKIN'S LYMPHOMA**Sevcenco V.,***student, Faculty of General Medicine
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Republic of Moldova, Chisinau***Abstract**

Hodgkin's lymphoma (LH) or lymphogranulomatosis is a neoplasia of the lymphatic tissue, which can affect people of different ages [1]. LH can appear in any decade of life, but most frequently at the age of 16-35 [2]. REED-Sternberg cells represent a pathognomonic sign for classic LH [3]. The clinical picture does not involve any specific signs [2]. Most patients present lymphadenopathy, and the lymph nodes most frequently are the primary focus [4]. The diagnosis is established by performing biopsy of the affected lymph node or the suspected organ. Epidemiological, clinical – evolutionary and diagnostic aspects of Hodgkin's lymphoma were studied in 60 patients, diagnosed with Hodgkin's lymphoma (HL), from the database of PMSI Oncologic Institute, Chisinau, Republic of Moldova. All the evaluated cases were morphologically confirmed. It was determined that HL developed more frequently up to the age of 35 years (41,7%). The recurrence of the appearance of HL by gender showed a prevalence of men - 53%, 32 patients out of 60.

Keywords: Hodgkin's lymphoma, diagnosis, epidemiology, symptoms, gender.

Introduction

Hodgkin's lymphoma (LH) is a neoplasia of the lymphatic tissue, which can affect people of different ages [1]. In this pathology there are Reed-Sternberg and Hodgkin cells, which on a background of inflammatory cells are surrounded by T lymphocytes [3].

The incidence of this neoplasia among all lymphomas is 24%. In 2020, globally, 0.4% and 0.2% of all reported deaths were caused by Hodgkin's lymphoma [5]. LH can appear in any decade of life, but most frequently at the age of 16-35 [2]. This lymphoma is rarely found in children under 5 years of age, but it is one of the most diagnosed types of cancer in adolescents aged 15-19 years. In the Republic of Moldova, the incidence of LH morbidity is 1.46 cases per 100,000 inhabitants, and the gender distribution is: men-1.53 and women 1.06. This index increases, reaching high values at the age of 50-60 years [1]. In 2021 HL was diagnosed in 10,04% cases of hematological malignancies [13]. According to a study carried out in 2020, the highest incidence was determined in Southern Europe (ASR=2.8), followed by Northern Europe (ASR=2.6), Australia and New Zealand (ASR= 2.6) and Western Europe (ASR=2.5) [5]. RS cells derive from the germinal center of B cells where antigen-dependent proliferation and selection of already mature B-lymphocytes. Upon antigenic stimulation during each division of the lymphoid cell changes occur in the immunoglobulin gene, the so-called "somatic hypermutations" which would normally get the signal to initiate apoptosis. But due to several oncogenic events, some of them avoid apoptosis, and begin to proliferate uncontrollably and become neoplastic cells [6]. Reed-Sternberg cells present on their surface the expression of CD30,

MUM1, CD15 and a weak expression of PAX5, which are used for differential diagnosis [7]. A mechanism by which tumor cells remain undetected by T cells is the genetic changes that occur after of the amplification of the JAK2 section of chromosome 9p24.1. The NF-κB pathway is also involved in tumorigenesis [8]. Studies on in situ hybridization have determined one of the clonal forms of the Epstein-Barr virus genome in RS cells in about 30% of the cases examined [6]. The clinical signs presented by the patient depends on: the stage of the disease and the spread of the neoplastic process [2]. Most often the lymph nodes of the cervical region are involved in about 50%, supraclavicular 25%, but the mediastinal and axillary ones are involved less often, with an incidence of 13% and 10% [1]. Systemic symptoms, which are also called "B symptoms", which have an influence on the patient's prognosis are: profuse night sweats, weight loss of about 10% of body mass in the last 6 months, fever higher than 38 °C at least 3 days in a row without signs of inflammation [9]. The diagnosis of Hodgkin's lymphoma is established by performing a biopsy of the affected lymph node or the suspected organ, with the identification of Reed-Sternberg cells and their morphological types on a reactive background consisting of inflammatory cells [6]. The immunophenotypic profile of Reed-Sternberg cells in the classical forms of LH are similar, they are positive for CD30, CD 15, IRF4/MUM1 and negative for CD45 and EMA. RS cells express PAX-5 in approximately all cases, but with lower intensity compared to the surrounding small neoplastic B cells [9].

The clinical stage, the presence of clinical signs and the presence of the tumor are the important factors in the prognosis of LH, and in addition the histology and the stage of the disease are widely used for risk

stratification and the choice of appropriate initial therapy. The prognosis is largely influenced by the stage of the disease [9].

Aim of the study:

Identification and evaluation of the epidemiological, clinical-evolutionary and diagnostic features of patients in different stages of Hodgkin's lymphoma.

Materials and methods

This manuscript is based on the observational, descriptive and cohort study. The study included 60 patients diagnosed with Hodgkin's lymphoma, from PMSI Oncological Institute of the Republic of Moldova from 2018-2022. The retrospective and prospective patients' groups were evaluated. The diagnosis was proved by histopathological and immunohistochemistry examinations. The histological type of Hodgkin's lymphoma was identified according to the criteria of the International Classification of Tumors of Hematopoietic and Lymphoid Tissue revised by the WHO in

2016. The patients' staging was performed or reviewed according to the criteria of Lugano Classification of Malignant Lymphomas. The patients' follow-up and studies were performed at the comprehensive cancer center and related to the hospitalized and outpatient care. The selected patients' data were compared at the step of inpatient admission and staging regarding the involved lymph nodes, histopathological, immunohistochemical and imaging investigations, etc. The following methods were used for the researches: epidemiological, descriptive and comparative statistics, clinical-analytical method.

Results

The patients included in the study are aged between 20 and 73 years, with a mean age of 43.03 years. There were observed a prevalence of patients aged up to 35 years -41.7%. Patients aged 36-50 years -31.7%. The lowest incidence was identified in patients older than 71 years - 6.7%. (Figure 1)

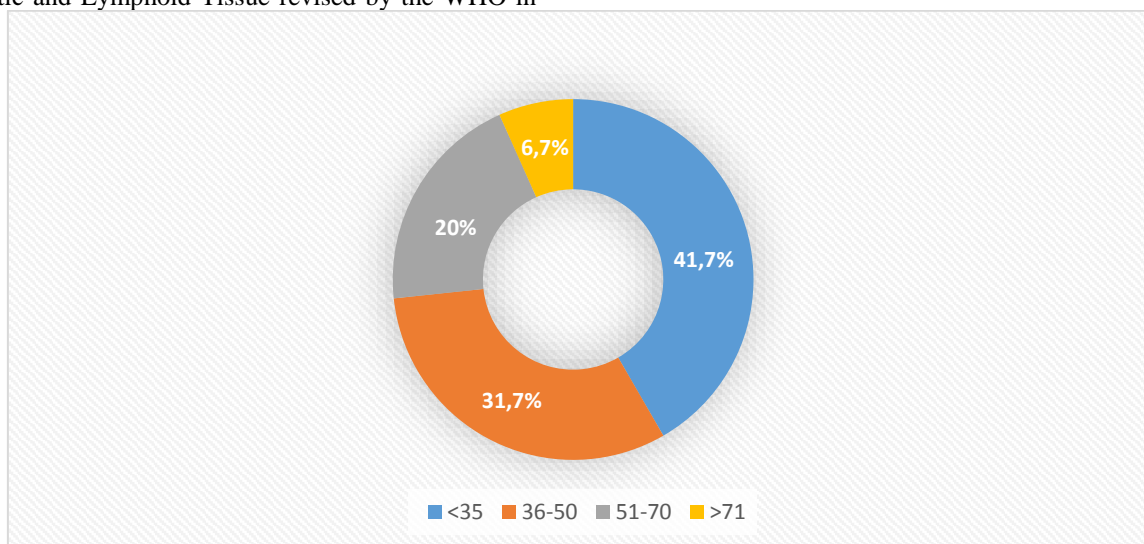


Figure 1. Distribution of patients with Hodgkin's lymphoma by age

In the gender distribution, we observed a male prevalence of 53%, and women 47%. (Figure 2)

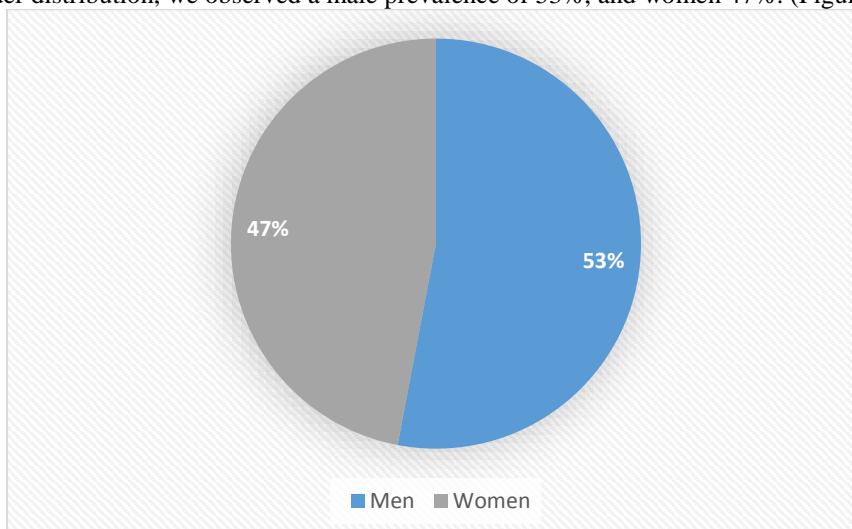


Figure 2. Distribution of Hodgkin lymphoma patients by gender

After analyzing all the signs presented by the patients, we identified the fact that the most widespread sign was the presence of a volume formation, represented by the affected lymph nodes, with an incidence of 83.3%. Other complaints encountered were general weakness -31.6%, pain syndrome - 30%, significant weight loss in a limited period of time and excessive night sweats - 21.6%, persistent skin itching - 16.6%, fever for a long time and with variable values - 15%, cough - 11.6%, dyspnea - 6.6% (Figure 3). All these accusations are due to the increase in volume of the affected lymph node, with changes in the architecture of the neighboring tissues, as well as the

spread of the neoplastic process in organs and tissues. The majority of patients -33 patients (55%) did not present any of the symptoms of group B such as: fever higher than 38 °C at least 3 days in a row without signs of inflammation, weight loss by 10% of body mass in the last 6 months, profuse night sweats.

Depending on the charges presented and due to the fact that the disease is asymptomatic for a long time, patients present themselves to the doctor in various stages of the disease's evolution, and it was determined that the most frequent patients go to the specialist in the advanced stages, i.e. stage IV -36,6%, stage III- 21.3%, stage II- 35%, stage I- 6.6%.

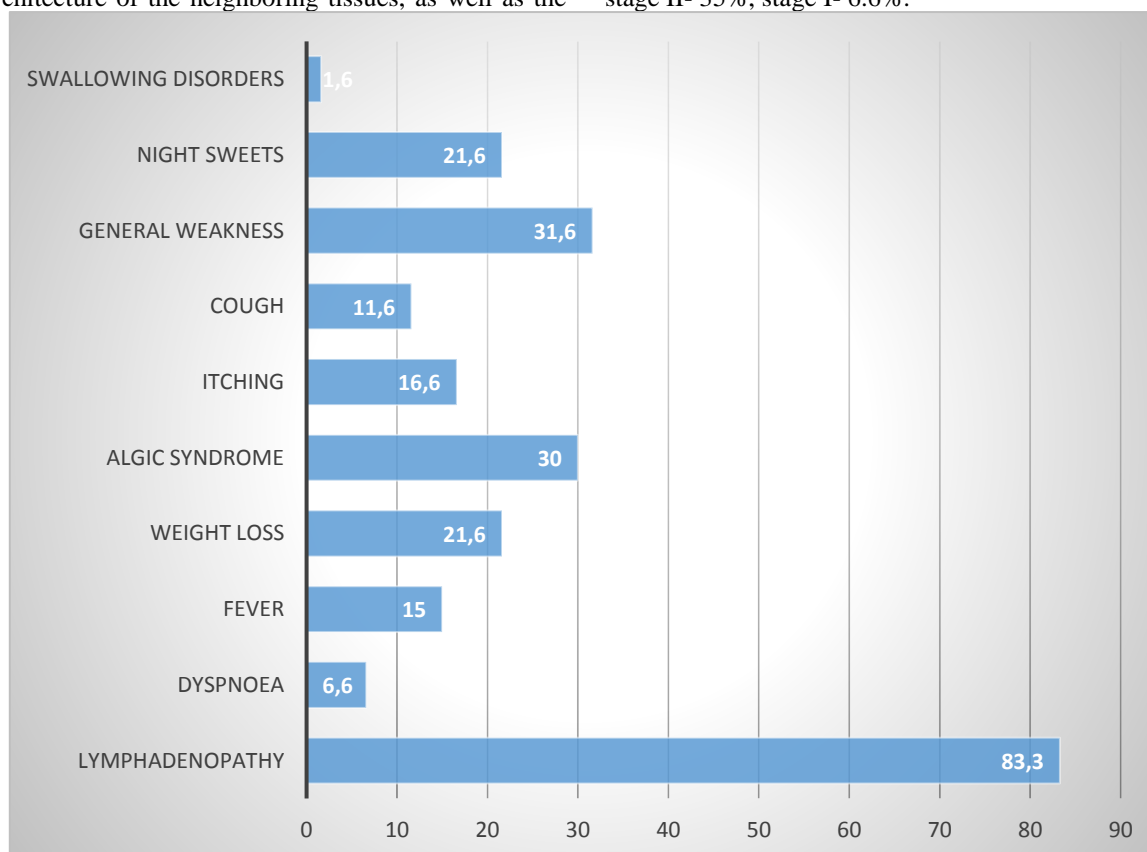


Figure 3. Distribution of patients with Hodgkin's lymphoma according to the charges presented.

After the analysis of the medical records, we identified the improvement of the condition in 42%, the progression of the neoplasia, despite the treatment carried out in 28%, the complete remission was determined in 22%, the relapse in 8% (Figure 4). Thus we can conclude that the evolution of the disease can be different and is influenced by several factors such as: the treatment used, the stage and spread of the disease, when the treatment was initiated, the presence

or absence of group B symptoms, the patients' compliance with the treatment, the comorbidities and complications that intervened both in the evolution of the disease and in during treatment. The prognosis is influenced by the risk factors present in patients, such as affecting more than 4 nodal areas - 48.3%, VSH greater than 50mm/h -35%, age greater than 50 years - 31.6%, mass mediastinal - 13.23%, ESR greater than 30 but with the presence of group B symptoms - 11.6%.

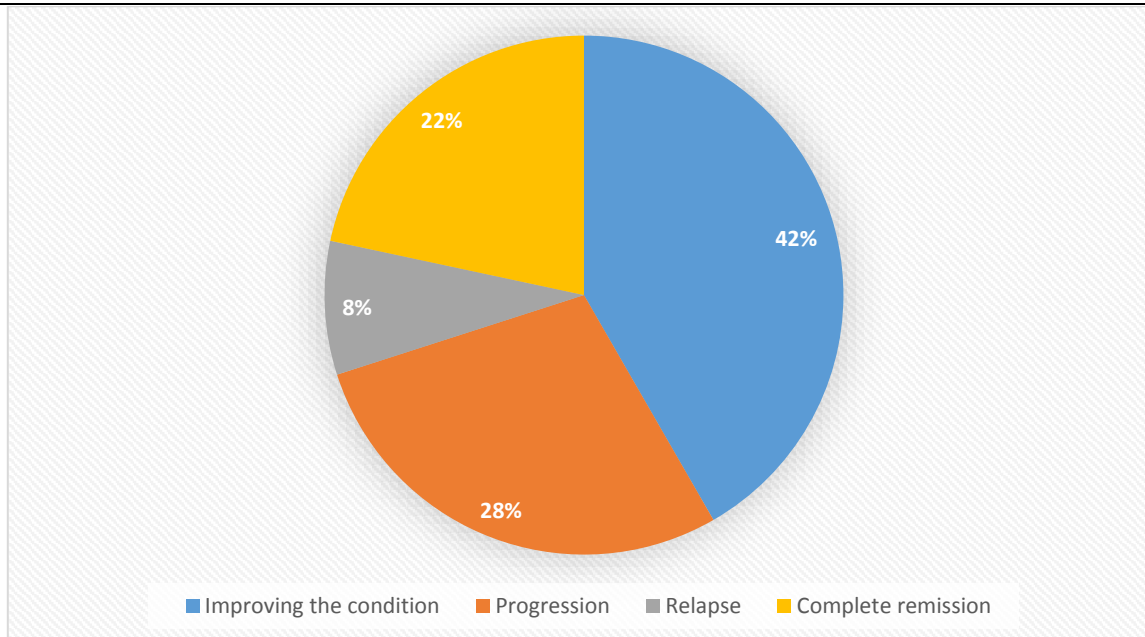


Figure 4. Distribution of patients with Hodgkin's lymphoma according to disease progression.

For differential diagnosis, immunohistochemical markers such as CD30 and CD 15 were used, which were identified in 58 patients, MUM1-33.3%, PAX5-30%, CD20-3.6%, CD45- 3.3%. After evaluating the morphological results, the most common form of LH identified was nodular sclerosis, identified in 66.7% of patients.

Discussion

Hodgkin's lymphoma is a malignant tumor of the lymphatic tissue that sometimes presents difficulties in diagnosis due to its long asymptomatic period.

It was determined that Hodgkin's lymphoma developed more frequently up to the age of 35 years (41.7%). The recurrence of the appearance of Hodgkin's lymphoma by gender showed a prevalence of men - 53%, 32 patients out of 60, these data correspond to a study carried out in 2020 regarding the global analysis of the incidence of HL, in which the male gender was about 50% higher than female [10]. Also in 2021, the incidence of Hodgkin's lymphoma was 2.0 [13]. In the 36.6% of the patients had stage IV of the expansion of the neoplastic process. In 55% of cases they were asymptomatic, and in 45% of patients presented the B symptoms - fever higher than 38 °C for at least 3 days in a row without signs of inflammation, weight loss by 10% of the body mass in the last 6 months, profuse night sweats. Similar results were also described in the study performed by Hatem Kaseb and Hani M. Babiker, in which the symptoms of group B were identified in a small proportion, about 30% of patients [3].

It is important to note that after the lymph node biopsy and carrying out the immunohistochemistry examination there was determined that CD30 and CD15 was found in 96.6% cases and it is typical for classic

HL, such result was illustrated in the article by H. Wang, J.P. Balakrishna, S. Pittaluga, and E.S. Jaffe, in which it is presented that the markers CD30, CD 15, EBV and MUM1 are characteristic of classic HL. However, CD 45 is positive only for NLP-HL. CD20 and PAX5 can be identified both in the classical forms and in the nodular form with lymphocytic predominance [11]. In the study, it was pointed out that after the treatment that was performed in 42% the condition improved, in 28% there was progression, in 22% complete remission, and in 8% relapse.

Detrimental risk factors are defined across the world by various cooperative groups. There was incorporated criteria such as an elevated ESR, presence of B symptoms, increased number of involved nodal sites and tumor bulk [12]. There was determined that the 5-year overall survival in the incipient stages – I and II is approximately 90%, however in the stage IV the 5-year overall survival is approximately 60% [3].

Conclusions

1. The most affected age group with Hodgkin's lymphoma is up to the age of 35 years (41.7%). The lowest incidence of these disease was identified in patients older than 71 years - 6.7%.

2. The most common complaints are general weakness (31.6%), pain syndrome (30%), significant weight loss in a limited period of time and excessive night sweats (21.6%), persistent skin itching (16.6%), fever (15%).

3. As a result of long asymptomatic period and the latent onset of the disease determined late referral of patients to the doctor, thus explains the prevalence of advanced stages in patients (36.6%).

4. Clinical signs, the stage of development of Hodgkin's lymphoma, the histological form, the risk factors will influence the evolution of the disease, the selected treatment and compliance to the treatment.

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