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RESEARCH OF FEATURES OF DEVELOPMENT OF EPIDEMIOLOGICAL SITUATION ON LYMPHOGRANULEMATOSIS IN UKRAINE

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Мета: *проаналізувати особливості розвитку епідеміологічної ситуації з лімфогранулематозу в Україні упродовж 2012–2018 рр.*

Матеріали і методи. *У дослідженнях використовувалися дані Національного канцер-реєстру за 2012–2018 рр..Застосовувалися історичний, аналітико-порівняльний, системний, логічний, гіпотетико-дедуктивний, математико-статистичний, також методи епідеміологічних досліджень.*

Результати дослідження. *Встановлено, що захворюваність тасмертність дорослого та дитячого населення від лімфогранулематозу, що виражені в абсолютних показниках упродовж 2012 р.–2018 р. в Україні знизилась. Так, кількість захворівших на лімфогранулематозу 2012 р. порівняно з даними 2018 р. зменшилась на 26,9 %, а смертність – на 41,2 %, серед дітей – на 37,7 % та 25,0 % відповідно. Всі абсолютні показники мали складний характер змін, з піковими значеннями даних у 2015 р. та 2018 р. (захворюваність дорослих),а також у 2016 р. (смертність дорослих) та 2015 р. (захворюваність дітей). При цьому, жоден показник так й не досяг та не перевищив значення даних 2012 р., окрім даних по захворюваності дітей на лімфогранулематоз у 2015 р. (збільшення на 11,8 % відносно попереднього 2014 р.). Вселяє оптимізм той факт, що після 2015 р. показники захворюваності дітей на лімфогранулематоз планомірно знижувалися. Доведено, що у сукупності показників захворюваності жинкипревалювали (53,4 %), а у структурі смертності навпаки питома вага (%) жінок була меншою (43,0 %). Серед дитячого контингенту хворих, більше було представників чоловічої статі (53,0 %). За даними аналізу відносних показників захворюваності серед чоловіків встановлено, що їх середнє значення (2,29 на 100 тис. населення) в Україні не перевищувало відповідні дані світової епідеміології (2,3 на 100 тис. населення) на лімфогранулематоз. Серед жінок середнє значення захворюваності (2,46 на 100 тис. населення) значно перевищувало відповідні світові показники (1,9 на 100 тис. населення). Середнє значення відносних показників смертності від лімфогранулематозу, яке було нами розраховано упродовж2012–2018 рр. дорівнювало для чоловіків 0,69, а для жінок - 0,47, проти світових даних 0,4 і 0,3 відповідно на 100 тис. населення. Таким чином, можна зробити висновок, що рівень чоловічої смертності у відносних показниках в Україні від лімфогранулематозу був більшим, ніж відповідні світові показники в 1,7 рази, а для жіночої популяції в 1,6 рази.*

Висновки. *З 2012 р. по 2018 рр. в України вдалося суттєво знизити показники захворюваності та смертності, що представлені в абсолютних даних. При цьому, викликає занепокоєння факт того, що у відносних показниках відбувається зростання захворюваності серед жінок, а також смертності від лімфогранулематозу серед дорослого контингенту хворих. Це дає змогу стверджувати про необхідність подальшого впровадження програм ранньої діагностики та схем хіміотерапії, які дозволяють підвищувати рівень 5-річної виживаності, а також досягти стійкої та тривалої ремісії для хворих*

Ключові слова: *епідеміологія, лімфогранулематоз, лімфоми, онкогематологія, хвороба Ходжкіна*

1. Introduction

Lymphogranulomatosis (LGM) or Hodgkin lymphoma is a relatively rare disease in comparison with other oncological diseases [1, 2]. In the structure of the general morbidity of the population of oncological pathologies, the weight (%) of patients with LGM is approximately 0.5–0.7 % [3, 4]. In economically developed countries, the incidence and mortality rates of LGM are 2.3 and 0.4 in men and 1.9 and 0.3 in women, respectively [5]. In developing countries, similar epidemiological rates are 0.8 and 0.4 in males and 0.5 and 0.3 in the female population. In general, the incidence data does not exceed 2–4 cases per 100 thousand population of the country [6]. Interesting are the results of recent studies by scientists regarding the evaluation of epidemiological indicators of LGM in accordance with various parameters, namely gender and race of patients, age, place of residence and social status [7, 8]. Scientists have shown that the risk of contracting LGM is higher in men than in women, as well as in patients with higher social and material status in society [9, 10]. Of particular importance in the etiology of LGM are genetic factors as well as Epstein Barr virus (EBV) [11, 12]. Scientists also consider the high likelihood of developing LGM in HIV

carriers, as well as in people with severe immune deficiency conditions, including congenital immune deficiency and organ transplant disorders and in those with bad habits, such as smoking [13, 14]. The greatest number of cases of LGM is observed in the age group of patients from 15 to 34 and from 50 to 60 years [15, 16]. At the same time, in the structure of the lymphoma, LGM makes from 30.0 % to 35.0 %, and in the age group of cancer patients from 15 to 34 years this diagnosis is made to every sixth patient [10, 17]. Scientists have shown that in 17.0 % of patients across all age groups progressive development of the disease is noted [7, 10].

The effective use of modern regimens of combination chemotherapy and radiotherapy have made it possible to significantly improve the effectiveness of treatment of patients with LGM, regardless of the course and stage of development of the pathological process [18, 19]. In economically developed countries, such an important indicator as the 5-year overall survival of LGM patients is, on average, 96.0 % [7, 10], and in Ukraine it is approximately 72.0–75.0 % [20, 21].

Clinical oncologists and haematologists are challenging increasing public demands for the efficiency of providing medical and pharmaceutical care to patients. Thus, previously the main criterion for the effectiveness of treatment of LGM or Hodgkin disease was considered the proportion (%) of patients with persistent remission [10, 20]. Nowadays, more and more attention is being paid to minimizing long-term side effects [22, 23].

With the paradigm shift in the treatment of LGM patients, it becomes increasingly important to analyse the epidemiological factors that affect the spread of this pathology in the world. Analysing the data of the specialized literature, we have established the fact that there are no studies on the epidemiology of LGM in Ukraine since the 2000s. Thus, in 2001 Kryvets D. Ya. presented the results of studies of the epidemiological situation with LGM for 1991–1998. [24] Given the above, as well as the socio-economic importance of improving the effectiveness of LGM treatment in the face of health care resource shortages in Ukraine, we have formulated the following research goal.

The aim of the research is to analyse in the dynamics of the years (2012–2018) the state of development of the epidemiological situation of LGM in Ukraine.

2. Planning (methodology) of the research

To achieve the stated aim of the study we have developed the following step-by-step tasks, the substantive content of which is presented in Table. 1.

Table 1

The main tasks and stages of the study

List of research objectives	Content of the main stages of research in accordance with their tasks
1	2
Determining the relevance of research	Analysis of the latest specialized literature outlining the problems of providing LGM patients with effective medical and pharmaceutical care was done. A thorough analysis of national sources and publications, which presents the results of epidemiological studies on LGM, as a basis for the formation of scientifically based models of medical and pharmaceutical support for the specified group of cancer patients under the conditions of the existing health care system in Ukraine was provided.
Outlining previously unsettled problems on the subject	According to the results of the systematization of the data of the relevant legislative and regulatory framework, as well as the data of the specialized literature over the last 10 years, issues that need further consideration on the way of forming scientifically grounded opinion regarding the introduction of the results of epidemiological research into practical medicine and pharmacy were identified. First and foremost it was done for the formation of rational models of pharmaceutical provision for LGM patients in the context of the shortage of resource support of national health system.
Determination of the aim, objects, tasks, basic methods of the research	According to the results of systematization of the literature data and considering the socio-economic importance of a complex of questions on improving the effectiveness of treatment of patients with LGM, which is solved, including based on scientifically grounded analysis of the dynamics of changes in epidemiological indicators, the research goal is determined. Objects, tasks and research methods are defined in accordance with the stated purpose of the work. The latter can be conditionally divided into general theoretical, which are used in applied research works and those used by scientists to solve problems with specific problems.
Collection of statistical material and its processing	Collection of statistics in accordance with the purpose and objectives of the study (National Cancer Registry of Ukraine – NCR, 2012–2018) was done. Epidemiological data such as the incidence and mortality of the LGM population in the dynamics of the years were selected, which are presented in absolute and relative (per 100,000 population) indicators. Necessary data processing was performed using standard statistical analysis packages Statistica (version 12.0, StatSoft, Tulsa, USA) and Excels preadsheet. A p-value <0.05 was considered statistically significant.

Continuation of Table 1

1	2
Analysis of the obtained results and their interpretation and discussion	According to the results of statistics collection, which reflect the status of the epidemiological situation of LGM in Ukraine in the course of years, conditional groups of indicators analysis are formed, namely: **the first group** (adult incidence of LGM in general and gender in absolute and relative terms); **the second group** (adult mortality from LGM in general and gender in absolute and relative terms); **the third group** (incidence of children from 0 to 17 years of age with LGM in general and gender in absolute and relative terms); **the fourth group** (mortality of children 0–17 years old by LGM as a whole and by gender in absolute and relative terms). There was a need to form analysis groups is due to the large number of statistics that have been selected for analysis. Thus, in the analysis ten sets of epidemiological indicators were used in the dynamics of years. Analysis and systematization of statistics according to the established groups of analysis allows determining the peculiarities of the epidemiological situation in different directions (morbidity, mortality, adult or child contingent of patients, gender, absolute and relative indicators, etc.).
Defining a range of restrictions on the use and interpretation of the results	Identifying the range of restrictions on the use and interpretation of research findings is based on an analysis of the balance between the practical possibilities of their use, including external and internal users of information in the context of existing health care system resources and the socio-economic significance of the problem under consideration in the short and medium term.
Formulating of conclusions and outlining directions for further research in that direction	According to the results of the analysis of the obtained results, after the evaluation of objective limitations regarding their use in practical medicine and the system of pharmaceutical supply (SPS) of cancer patients, the main conclusions and directions of prospective researches on the specified topic were formed.

3. Materials and methods

In accordance with the outlined goal and the developed research plan, the object of research was selected - data presented in the NCR of Ukraine for 2012–2018 [25]. As you know, NCR is a modern program-information system for the registration of oncological pathologies by their location and stages of development, which was started by the Ukrainian Research Institute of Oncology and Radiology (National Cancer Institute nowadays) in 1989.

Thanks to the introduction of this software product is able to systematically analyze the data of oncologic pathology registration in Ukraine according to different parameters in the dynamics of years. Given the fact that the formation of the NCR uses a single methodological approach to the analysis of the epidemiology of LGM in the dynamics of the years is justified. For analysis, we have selected the following epidemiological indicators of LGM over the years:

– Adult incidence of LGM in and in terms of gender - absolute value, number of persons (**first group** indicator);

– Adult incidence of LGMs as a whole by population and by gender - relative per 100,000 population according to WHO international standard (**first group** indicator);

– Adult incidence of LGMs as a whole by population and by gender - relative per 100,000 population according to Ukrainian Standard 2000, (**first group** indicator);

– LGM adult mortality rates in general by population and by gender - absolute value, number of persons (**second group** indicator);

– LGM adult mortality in population and gender breakdown - relative value per 100,000 population by WHO international standard (**second group** indicator);

– LGM adult mortality in population and gender breakdown – relative value per 100,000 population by Ukrainian Standard 2000 (**second group** indicator);

– morbidity of the child contingent (from 0 to 17 years) as a whole by population and by gender – absolute value, number of persons (**third group** indicator);

– incidence of infant population (from 0 to 17 years) as a whole by population and by gender - relative per 100 thousand population (**third group** indicator);

– LGM infant mortality rate (from 0 to 17 years) as a whole by population and by gender - absolute value, number of persons (**fourth group** indicator).

– LGM infant mortality rate (0–17 years) by population as a whole and by gender - relative per 100,000 population (**fourth group** indicator).

As we can see, the first and second groups included the incidence and mortality rates of LGM adults in absolute and relative terms, standardized to the requirements of WHO and the Ukrainian Standard in 2000, and the third and fourth similar epidemiological indicators in children, that is presented in absolute and relative terms per 100 thousand population of the country. The calculation of epidemiological indicators according to the "Ukrainian standard" in 2000, is carried out in the NCR on the basis of the age structure of the population of the country according to 2000. These epidemiological indicators, as indicated in the document, should be used to compare the incidence rates of different regions of Ukraine or to study the dynamics of incidence in the region [25]. It should be noted that since 2014, all epidemiological indicators are

presented without taking into account data on the Autonomous Republic of Crimea, Sevastopol, as well as individual territories of Donetsk and Luhansk regions, which are not under the control of Ukraine.

Historical, analytical, comparative, systemic, logical, hypothetical-deductive, mathematical-statistical, methods of epidemiological studies, etc. were used in the study. The analysis of epidemiological indicators used growth rates (%) as well as growth / decline coefficients (k). In the absence of operational data in the NCR Ukraine by the number of sick and dead in 2019, we, using the calculation and analytical methodology, predicted these indicators [26]. The compliance of the predicted morbidity and mortality rates of LGM patients with the actual data can be verified after the official publication of the NCR of Ukraine in 2022. This is due to the peculiarities of the epidemiological indicators in the NCR in the dynamics of years. Thus, the refined data in 2020 are displayed for 2018, and the operational data for 2019. Based on the results of the comparisons made, it will be possible to conclude on the adequacy of methods for predicting the incidence and mortality of LGM patients in Ukraine for 2019.

The calculations used both the chain data (the ratio of the indicators of the next to the previous period) and the baseline (the ratio of the data of a certain period to the similar indicators of 2012, which in the analysis had the status of the base year).

4. Results of the research

Based on the analysis of the first group of epidemiological indicators, we have established the following. Since 2012, there has been a systematic decrease in the absolute number of LGM patients (Fig. 1). Thus, since 2012 (1,176 people), their number has decreased by 26.9 % in 2018. During the study period, the average value of kavg was 0.9. A slight (3.0 %) increase in the number of LGM patients compared to the previous 2014 was observed in 2015 (959 people). Based on the analysis of the dynamics of population morbidity at LGM and using the calculation-analytical method of forecasting statistical indicators, we determined their number for 2019. Thus, this indicator was equal to the value of 775 people, which is 9.88 % less than in the previous 2018 and 34.1 % less than the base in the analysis of 2012.

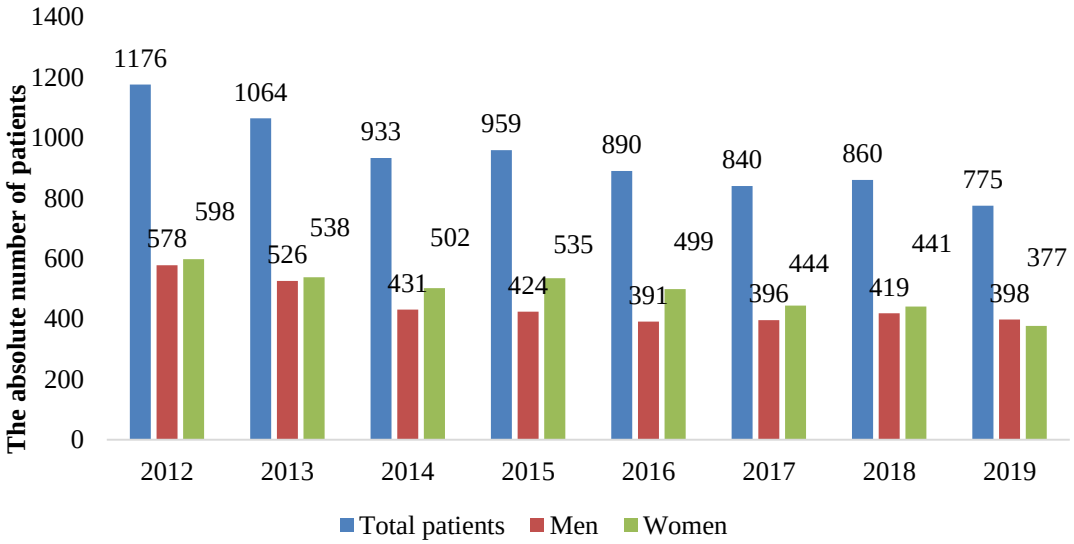

Fig. 1. The results of the analysis of the dynamics of changes in the incidence rates of the population of Ukraine during 2012–2018 for LGM and their forecast for 2019

The analysis of the dynamics of gender incidence showed the following features of the development of LGM epidemiology in Ukraine. Among men, there was a complex pattern of changes in the absolute incidence of LGM. Thus, for the period from 2012 to 2016, the corresponding indicators systematically decreased from 578 to 391 people, and then in 2016 and 2017 they increased. The average value of kavg was 0.95. For women, there was a somewhat different dynamic in the development of absolute rates of LGM incidence. Thus, the decline in morbidity data continued, compared to the male population, in a slightly shorter period, i.e. from 2012 to 2014. According to 2015 data, the number of LGM women increased by 33 or 6.6 %, and the positive dynamics of the decrease of the epidemiological parameters being investigated are further determined. The average value of kavg in all indicators during 2012–2018 was 0.95. Overall, it should be noted that the number of LGM cases in men in 2018 decreased by 27.5 % compared to the same data in 2012 and by 26.3 % in women.

Next, we conducted a structural analysis of the set of LGM patients in Ukraine by gender. The results of the analysis are presented in Fig. 2.

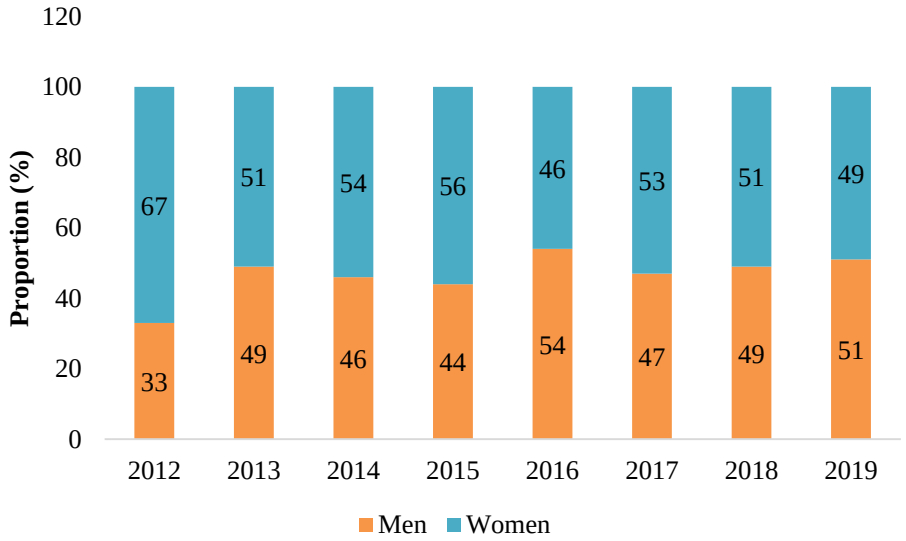

Fig. 2. Results of structural analysis of the LGM population during 2012-2018 (results of forecasting of relevant indicators in 2019)

As stated earlier, scientists have shown that men have a greater tendency to become ill with LGM than women [7, 9] According to a structural analysis of the incidence rates of LGM population, we have shown that during the period studied the proportion (%) of men fluctuated in the range values from 33.0 % (2012) to 54.0 % (2016). The average proportion (%) of men in the total population of ill people with the GLM was 46.6 %, respectively, of women – 53.4 %. Noteworthy is the presence of structural shifts in the absolute incidence rates of men in 2018, compared with 2012 data. Thus, the structural shifts were 18.0 %. In general, it should be noted that during 2012-2018 the zigzag dynamics of the epidemiological indicators under consideration were observed. For example, in the period from 2013–2015, the proportion (%) of LGM-infected men declined steadily, and in 2016 a structural shift of + 10.0 % was observed, followed by a decrease to –7.0 % (2017/2016). In 2018, there was a slight (2.0 %) increase in the proportion of men in the LGM population.

The relative incidence rates of the population of Ukraine, calculated by WHO standards during 2012–2018, ranged from 2.2 to 2.6 in the population as a whole, among men from 2.1 to 2.4, and from women to from 2.3–2.6 per 100 thousand population of the country. According to the analysis of morbidity among men, it was found that their average value (2.29 per 100 thousand population) in Ukraine did not exceed the relevant data of the world epidemiology (2.3 per 100 thousand population) for lymphogranulomatosis [7, 10]. Among women, the average incidence rate (2.46 per 100,000 population) was much higher than the corresponding world rate (1.9 per 100,000 population).

According to the incidence rates presented in the NCR of Ukraine and calculated according to the "Ukrainian Standard" in 2000, the epidemiological situation for LGM developed in the following values: in general for all patients from 2.4 to 2.7 persons per 100 thousand population; for men – from 2.3 to 2.7 persons per 100 thousand population; for women – from 2.4 to 2.9 persons per 100 thousand population.

The second group of epidemiological indicators was formed by data on mortality of patients with LGM. The results of the analysis of this set of patients are presented in Fig. 3. The number of LGM deaths in Ukraine since 2012, as well as absolute morbidity rates, have also reduced the trend towards a systematic decline, from 401 to 236 people in 2018, or 41.2 %. Against the background of a systematic decrease in data during 2012–2015, the number of deaths from LGM in 2016 by 17 persons (+ 6.9 %) is noteworthy. At the same time, in the next 2017 and in the future we observed a decrease in mortality data from the specified oncohematological pathology. The average value of kavg for all indicators during 2012–2018 was 0.91, and for men, kavg=0.95, and for women, kavg=0.90. That is, it can be argued that in the female population, mortality rates were declining at a higher rate than among men.

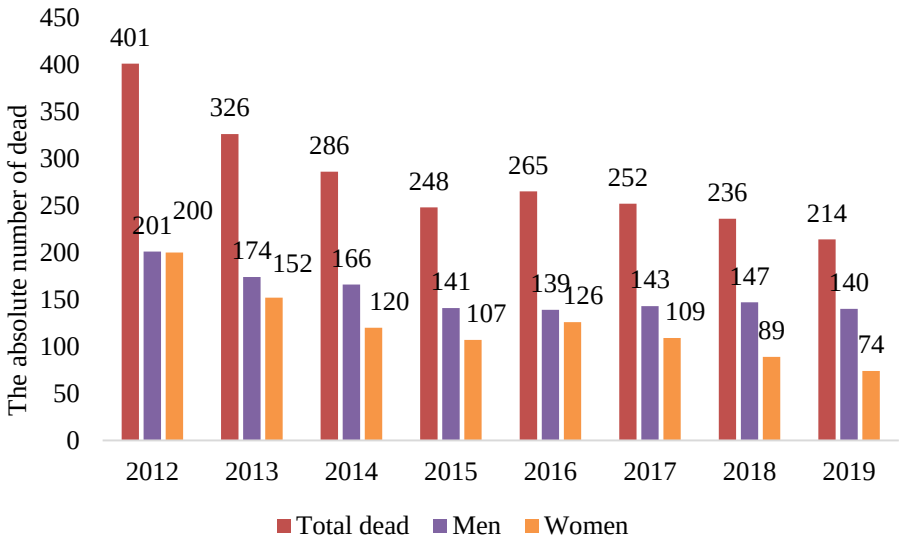

Fig. 3. Analysis of the dynamics of change and structure of the population (gender) of LGM deaths during 2012–2018 (2019 results of forecasting relevant indicators) in Ukraine.

It should be noted that the greatest decrease (%) of death rates of patients with LGM was observed in 2013. Thus, the total number of deaths from LGM decreased from 401 people to 326 people, i.e. by 18.70 %. If we analyze the dynamics of population mortality in accordance with gender, then we can determine the following characteristics of its changes. Among men, the fall in mortality was observed over a longer period compared to women, namely from 2012 to 2016 (absolute mortality rates decreased by 30.9 %), followed by a 2.8 % increase in 2017 and 2018, respectively. Among women, a significant decrease in absolute mortality rates by almost 2 times was observed during 2012–2015 (from 200 to 107 persons, ie almost 2 times). In the following 2016, the death toll of LGM women increased by 17.8 %, and in the following 2017 and in 2018, we observed a decrease of 13.50 % and 18.35 %, respectively. Overall, the total number of LGM deaths in 2018 has decreased by 26.9 % compared to 2012 and by 2.25 times among women.

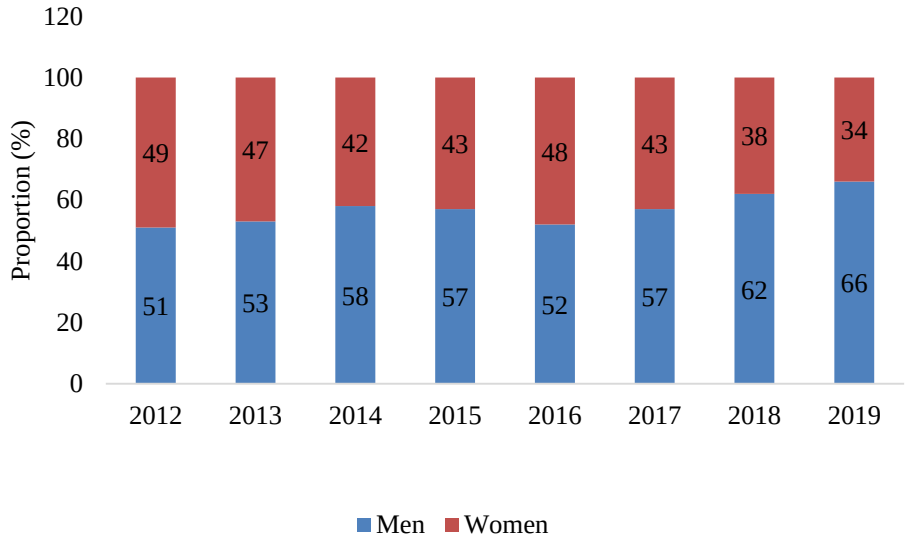

Fig. 4. Results of structural (gender) analysis of LGM patients (2012–2018 according to NCR and 2019 – results of forecasting relevant indicators)

The relative mortality rates of LGMs (per 100,000 population) were then analyzed. Thus, mortality rates, calculated by WHO standards, ranged from 0.6 to 0.8 for all the dead, among men – from 0.8 to 1.0, women – from 0.5 to 0.8 per 100,000 population of the country. The average LGM mortality rate calculated during 2012–2018 was 0.69 for men and 0.47 for women, against 0.4 and 0.3 for the world population, respectively, per 100,000 population. Thus, it can be concluded that the level of male mortality in relative figures in Ukraine by LGM was higher than the corresponding world indicators by 1.7 times, and for the female population by 1.6 times.

According to epidemiological data presented in the NCR of Ukraine and calculated according to the Ukrainian Standard in 2000, the LGM mortality statistics

were as follows: for all deaths from 0.6 to 0.8 per 100,000 population; for men – from 0.8 to 1.0 persons per 100,000 population; for women – from 0.5 to 0.8 people per 100,000 population.

The third and fourth group of indicators characterized the development of the epidemiological situation in the pediatric contingent of patients (0 to 17 years).

Figures 5 and 6 show the results of the analysis of dynamics (2012–2018) and forecasting for 2019 of the incidence of infant population with LGM, expressed in absolute data.

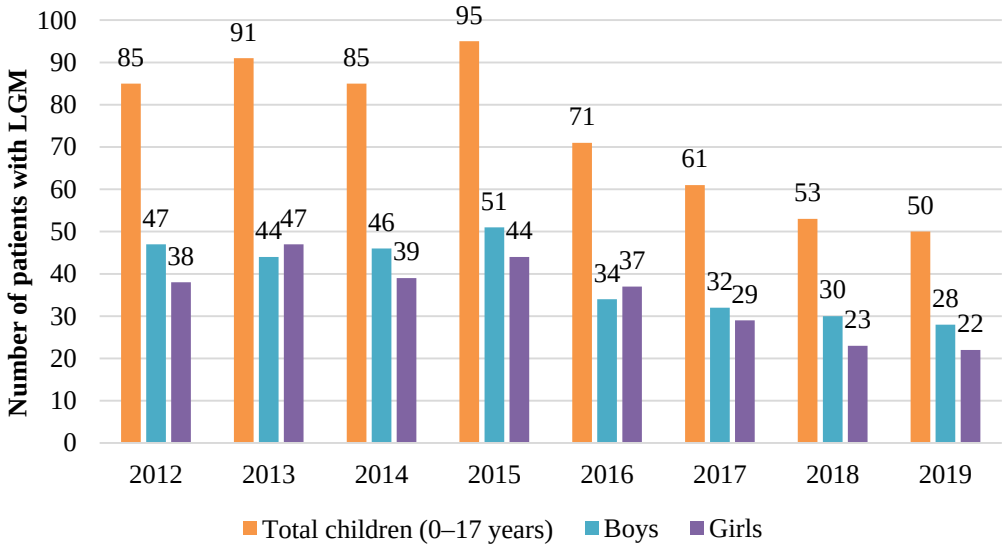

Fig. 5. Analysis of the dynamics of the incidence of child population of Ukraine on LGM during 2012–2019, including for 2019 – forecasting results

As we can see, there is a positive trend in Ukraine in reducing the absolute morbidity data from 85 in 2012 to 53 children in 2018, ie by 37.7 %. It should be noted that, unlike similar indicators for the adult population, which did not rise above the 2012 data during the whole study period, we observed a peak incidence of the incidence of 95 children with LGM in 2015. It is noteworthy that in the same year, the number of children with LGM was the highest during the entire observation period (2012–2018). It should be noted that the increase in the number of patients in 2015 compared with the data of the previous 2014 was also characteristic of the adult contingent of patients. It should be noted that during 2012–2015 the zigzag character of the change in the absolute rates of child morbidity at LGM was observed, and only from 2016 did their number begin to decline systematically. Thus, in 2016, this indicator decreased by 25.3 % and was equal to 71 cases against 95 children in 2015. The absolute morbidity, represented by gender of LGM patients, was similar. The highest growth rates (+ 23.1 %) in the dynamics of indicators were characteristic for girls in 2013 (47 persons) against the data of the base year 2012 (38 persons), and the lowest (–33.3 %) for boys in 2016 (34 patients), compared with 2015 data (51 patients).

In accordance with the gender structure (mean data for 2012-2018), children with LGM were as follows: 53.0 % (boys): 47.0 % (girls). For comparison, the same average for the adult contingent was 46.6 % (males): 53.4 % (females).

The proportion (%) of boys in the total LGM population by years ranged from 48.0 % (2013, 2016) to 57.0 % (2018). Relative morbidity rates (per 100,000 population) ranged from 0.8 (2018) to 1.4 (2015). For the cohort of boys, the reported morbidity rates were 0.9 (2018 and 2017) – 1.5 (2015), and girls: 0.7 (2018) – 1.3 (2015).

Analyzing child mortality (the fourth group of epidemiological indicators), it can be stated that these statistics do not go beyond 6-year-old sick children per year. Thus, in the aggregate of LGM patients, the mortality rate fluctuated over the 2012-2018 range in the following range (absolute data):

– total for LGM deaths - from 1 patient in 2018 to 6 patients in 2015 and 2016, respectively

– among boys – from 0.0 deaths according to 2018 data to 5 patients in 2015.

– in a cohort of sick female children - from 1 child in 2012 and 2018 to 3 patients in 2014 and 2016, respectively.

In the 100,000 population estimates, these mortality rates ranged from 0.0 to 0.1 for different years of the study (total in 2016, boys in 2015–2017, and girls in 2016 and 2018).

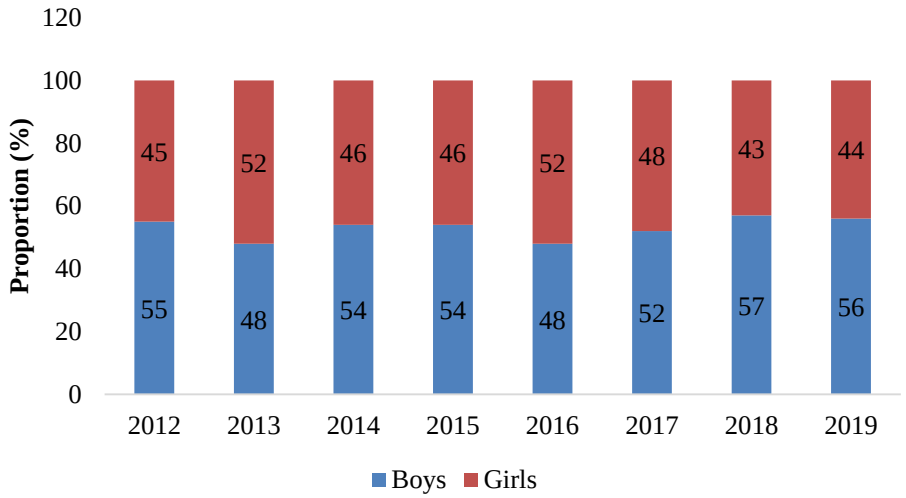

Fig. 6. Structural analysis of LGM sick children in 201–-2018, including 2019 data (morbidity prediction results) by gender

In the absence of NCR Ukraine data for 2019, for objective reasons, we further predicted LGM morbidity and mortality. Thus, in the adult contingent of patients, morbidity in absolute terms compared to the data of 2012 may decrease by 34.1 % (to 775 people against 1176 patients in 2012), the death rate of adult patients – by 46.6 % to 214 people against 401 patients in 2012. Among children, the incidence may be reduced by 41.2 %, i.e. up to 50 children against 85 LGM patients in 2012. Given the fact that the domestic health care system and the country as a whole is experiencing the effects of systemic the crisis that was observed during 2014–2015, this forecast looks optimistic and allows to confirm the existence of positive structural changes in the organization of early detection, effective diagnosis and provision of medical and pharmaceutical assistance to LGM patients in Ukraine.

5. Discussion of the research results

The following conclusions can be drawn from the results of the studies conducted by different groups of LGM epidemiological indicators in Ukraine during 2012–2018. First, all groups of absolute indicators show a positive and encouraging tendency to reduce both the morbidity and mortality of the population, including the infant contingent of patients. Among adults, the incidence from 2012 to 2018 declined by 26.9 % and the mortality rate by 41.2 %, among children by 37.7 % and 25.0 %, respectively. The only exception to this is the data on the pediatric contingent of patients according to the indicator of the third group, namely the incidence by absolute indicators in 2015. This year, as previously indicated, the incidence was higher than the data in 2012 by 11.8 %, compared to 2018 data, by 79.0 %. At the same time, the fact that after 2015 these indicators of morbidity among children have been steadily decreasing increases the optimism. All of the above data were complex in nature, with peak data in 2015, 2018 (adult morbidity), 2016 (adult mortality), and 2015 (child morbidity).

Second, taken together of absolute morbidity rates, the average number of female patients prevails (53.4 %), and in the structure of mortality, by contrast, the proportion of women was lower (43.0 %). Among the infantile contingent of patients, male representatives dominate (53.0 %). According to the literature, men are more likely to ill with LGM [7, 10]. The presence in Ukraine of something different from the global tendency in the gender distribution of LGM patients may be conditioned by the peculiarities of the demographic situation in the country, first of all the dominance of women in the structure of age groups (from 50 years and above), as well as the low life expectancy of men in general.

Third, comparing the relative epidemiological indicators (per 100,000 population) for LGM presented in studies from 1991 to 1998 in the works of domestic scientists (Krivets D. Ya., 2001) [24] about the following. For example, in 1991–1998 the average incidence of LGM (calculated according to the WHO international standard) in men was 2.83, and in 2012–2018 – 2.29 per 100,000 population, that is, according to the specified epidemiological index was observed positive downward trend. In women, on the other hand, the average incidence rate increased from 2.34 during 1991–1998 [24] to 2.46 per 100,000 population, according to 2012–2018. Also noteworthy is the fact that comparing the results of self-conducted studies with those that characterize the status of the epidemiological situation of LGM in the world the following should be noted. According to the relative morbidity rates among men, the average value (2.29 per 100 thousand population in Ukraine) did not exceed the global values (2.30 per 100 thousand population) of epidemiological indicators for LGM, and among women (2.46 per 100 thousand population), on the contrary, significantly exceeded the world indicators (1.9 per 100 thousand population). A similar statement can be made for mortality rates for both male and female cohorts of LGM patients. Thus, the average LGM mortality rate calculated for us in 2012–2018 was 0.69 for men and 0.47 per 100 thousand for women, 0.4 and 0.3 respectively for world data that is, the male mortality rate in Ukraine by LGM is higher than the world by 1.7 times and the female death rate by 1.6 times. This fact is of concern, given the recent advances in oncohematology toward increasing the 5-year survival rate of LGM patients and achieving stable remission [27, 28], as well as

the scientist's proven influence between direct and indirect economic losses and the progression of the indicated oncology [29].

The results of epidemiological studies on any nosology are the basis for the formation of rational models of organization of medical and pharmaceutical support of the population. Analysing the results of epidemiological studies on LGM over the years, we have identified the following restrictions on their effective use in theoretical and practical medicine and pharmacy. First, it is necessary to carry out additional studies on gender of sick and deceased LGM patients, taking into account the peculiarities of the demographic situation that has developed in recent years in the country. Thus, during 2014–2015, Ukraine experienced not only a systemic crisis but also socio-demographic upheavals that had a significant impact on society as a whole. Therefore, the presence of features of the epidemiological situation of LGM in Ukraine, in comparison with the world data presented in the specialized literature, creates a certain limitation on the way of their use in practical medicine and the process of pharmaceutical provision of cancer patients.

Given the fact that scientists have determined that there are two age-related increases in the incidence of LGM (15 to 24 and 50 to 50 years) [15, 16], the lack of results in these areas also causes limitations in their practical use.

Another factor that may, in our opinion, influence the objective interpretation of research results is the lack of a comparative analysis of similar studies from 2000-2011. As previously stated, similar epidemiological studies were conducted only in 2001 [24]. Unconditional is the fact that in order to form a reliable estimate of the development of the onco-epidemiological situation in the dynamics of years, the presence of continuous studies is necessary and appropriate.

Given the geographical, socio-economic and infrastructural differences of different regions of Ukraine, the analysis of changes in epidemiological indicators by LGM is relevant. The expediency of this direction of research seems promising given the fact that scientists have proven the importance of the influence of geographical factors on the epidemiology of LGM [4, 7].

The analysis of the dynamics of changes in epidemiological indicators, which are expressed in absolute terms, also requires additional studies, taking into account the fact of the loss of the Autonomous Republic of Crimea and certain Donetsk and Luhansk regions. Moreover, in 2015–2016, despite the loss of control, including epidemiological in these territories and because of the decrease in the statistical base of studies, the number of adults among adults in 2016, compared to 2015 data, it increased by 6.8 %, and among children in 2015 compared to 2014 – by 11.8 %. Therefore, conducting studies without taking into account regional peculiarities of the epidemiological situation in LGM, emigration processes, what is happening in the country is important, especially in the dynamics of the years.

Study limitations. Analysing the results, we can identify the following limitations on their practical use and interpretation. Therefore, more research is needed in the following areas:

– by gender of LGM patients and deceased patients, taking into account the particular demographic situation that has developed in recent years in the country;

– by age group of patients, especially considering the fact that there are two peak age-related rates of increase in the incidence of LGM (from 15 to 24 and from 50 to 50 years) [15,16];

– by administrative and territorial units of the country;

– in the dynamics of the years, taking into account the loss of epidemiological control in the Autonomous Republic of Crimea and in separate territories of Donetsk and Luhansk regions.

Prospects for further research. Analysing the results of the research and limitations on their use in the development of rational models of medical and pharmaceutical support to the population, we identified the following areas of prospective research: conducting factor analysis of the influence of external and internal parameters on the dynamics of changes in epidemiological indicators of LGM; research of the gender structure of sick and deceased patients in the context of development of socio-demographic situation in Ukraine; study of the epidemiology of LGM in accordance with the administrative and territorial division of the country, as well as the infrastructure, from the medical and pharmaceutical point of view, the possibilities of development of its individual regions; analysis and prediction of the incidence and mortality rates of LGM patients at age intervals among the female and male cohorts of LGM patients.

6. Conclusions

At the end of the research it should be noted the following. Despite the systemic crisis experienced by the country during 2014–2015, as well as the current challenges to the need for a restructuring of the healthcare system and the formation of patient-oriented models of relations between the state and consumers of medical and pharmaceutical services in the country, it has been possible to significantly reduce the incidence, more importantly, in our view, mortality in absolute numbers of LGM adults and children. However, in terms of relative indicators, there is concern about the increase in morbidity among women, as well as mortality from lymphogranulomatosis among the adult contingent of patients. This makes it possible to state the need for further implementation of early diagnosis programs and chemotherapy regimens that improve the 5-year survival rate of patients and achieve sustained and long-term remission.

Conflict of interests

There is no conflict of interest.

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