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BLADDER CANCER: FEATURES OF EPIDEMIOLOGY AND INDICATORS OF SPECIALIZED CARE DELIVERY

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Ключові слова: *рак сечового міхура, поширеність, захворюваність, профогляд, показники результативності спеціалізованої допомоги*

Ключевые слова: *рак мочевого пузыря, распространенность, заболеваемость, профосмотр, показатели результативности специализированной помощи*

Abstract. Bladder cancer: features of epidemiology and indicators of specialized care delivery. Saidakova N.O., Yatsina O.I., Grodzinsky V.I., Stus V.P., Polion M.Y., Shiloh V.M., Kononova G.E. *The work is based on the materials of official statistical reporting, the analysis of which was carried out for 10 years, divided into two five-year periods (2009-2013 and 2014-2018). Absolute and intensive rates of morbidity and spread of bladder cancer in the adult population of Ukraine in the regional aspect, taking into account sex were studied, the basic indicators of the prevalence of pathology were analyzed as well. The revealed unfavorable situation is characterized by a steady increase in morbidity and prevalence at a lesser pace during 2014-2018. It is noteworthy the high level of morbidity in men, which is growing against the background of its stabilization in women. At the same time, there was noted the tendency in the reduced number of newly diagnosed patients during professional examinations (in 2018-16.9% against 18.0% in 2014) with diagnosis at stages I-II (72.2% vs. 74.79%), wherein every fifth has stage III-IV. With a tendency to increase in the number of registered patients ≥ 5 years (59.1% vs. 56.5%), the death rate did not change significantly within a year from the time of diagnosis (14.7% vs. 15.6%, respectively). In the structure of specialized care, 65% are newly diagnosed patients, surgical method accounted for 37-40% by years, the combined was second (up to 20% by years), then radiation and chemotherapy, which together did not exceed 5.0%. Areas with high or low relative rates*

regarding to the average Ukrainian indicators for all studied parameters were identified. In the presence of regional differences, there is a need for in-depth studies of the state of the issue, including the quality and organization of care.

Реферат. Рак мочевого пузыря: особенности эпидемиологии и показателей специализированной помощи больным. Сайдакова Н.А., Яцына А.И., Гродзинский В.И., Стусь В.П., Полион Н.Ю., Шило В.Н., Кононова Г.Е. Работа основывается на анализе материалов официальной статистической отчетности за 10 лет, которые были разделены на два пятилетия (2009-2013 гг. и 2014-2018 гг.). Изучались абсолютные и интенсивные коэффициенты заболеваемости распространенности рака мочевого пузыря среди взрослого населения Украины в региональном аспекте с учетом пола, анализировались также основные показатели результативности специализированной помощи. Выявлена неблагоприятная ситуация, которая проявляется устойчивым ростом заболеваемости и распространенности с меньшим темпом в течение 2014-2018 годов. Отмечен высокий уровень заболеваемости мужчин, который растёт на фоне стабилизации его среди женщин. Одновременно обнаружена тенденция к уменьшению впервые выявленных больных во время профосмотров (в 2018 г. – 16,9% против 18,0% в 2014 г.) с диагнозом на I-II стадиях (72,2% против 74,79%), при этом у каждого пятого на III-IV стадии. При тенденции к увеличению зарегистрированных больных ≥ 5 лет (59,1% против 56,5%), не существенно изменился показатель умерших до года с момента установления диагноза (14,7% против 15,6% соответственно). В структуре специализированной помощи (65% приходится на больных с впервые выявленным диагнозом) на хирургический метод приходилось 37-40% по годам, на втором месте – комбинированный (до 20% по годам), за ним лучевой и химиотерапевтический, что вместе не превышало 5,0%. Выявлены области с высокими или низкими показателями, относительно среднеукраинских, по всем изучавшимся параметрам. При наличии региональных различий возникает необходимость в углубленных исследованиях этого вопроса, в том числе качества и организации помощи.

Timely diagnostics and adequate treatment with subsequent careful monitoring of patients remain constant issues of modern oncology [7, 10]. They are to the full related to bladder cancer (BC), especially in recent years methods of treating this pathology have been improved. Their choice and effectiveness are subject to determining the histological type of the tumor, assessing the depth of innovation and the degree of malignancy [4]. The above-mentioned defines the determination of reliable verification of the diagnosis. However, despite the existing efforts to find new methods of imaging, the involvement of tumor markers aimed at detecting cancer process in the early stages, the frequency of recurrences is a serious problem. Under such conditions, purposeful organizational measures in the form of intensification of professional examinations, as well as wide awareness of the population with the formation of responsibility for their own health can be important [8, 11]. At the present stage of intensification of various spheres of activity, rhythm and way of life, changes in the environment, demographic features, which, as etiological factors, are related to epidemiological processes, it is important to have constant knowledge of their dynamics [2]. The results of the evaluation of the activity of the medical care delivery in relation to the management of such patients are no less significant. The dynamics of its indicators will allow to critically characterize the problem state and define perspective directions concerning scientific developments and of actually clinical practice [3, 11]. Such information is especially important not only in Ukraine, but also in some of its

administrative territories. They should motivate the study of risk factors at local level, which will provide an opportunity to take into account and influence some of them, to develop real measures to change the situation [9, 13].

The above-mentioned determined the purpose of this work. It consisted in studying (over 10 years) the prevalence, incidence of BC, taking into account gender, as well as the main indicators of specialized care delivery to this contingent in the regional aspect.

MATERIALS AND METHODS OF RESEARCH

The data of official and branch statistical reports were used in the work: Form No. 7 "Report on the incidence of malignant neoplasms", Form No. 35 "Report on the contingent of patients with malignant neoplasms", Form No. 47 "Report on the network and activities of medical institutions". The study period was 2009-2013 and 2014-2018, with two five-year plans set aside to determine not only the nature of process changes but also their intensity. Note that in the last five years, for obvious reasons, the data have been limited due to the lack of them from the currently uncontrolled territories. Absolute and relative values were studied. Levels of morbidity and prevalence of BC are given per 100 thousand of the relevant population. Time series were characterized by standard indicators: absolute increase (decrease), growth rate (decrease). The internal structure of the phenomena was analyzed, the determined average values of the indicators were compared with their standard error.

Statistical processing and analysis of results were performed according to generally accepted methods

using licensed statistical analysis programs Statistica v.6.1 (StatSoft Inc., license No. AGAR909E415822FA) and Microsoft Excel. If it is necessary to identify the reliability of two parameters, the standard Student's t test was used [1, 5].

RESULTS AND DISCUSSION

According to the comparative analysis of absolute and relative values, which assessed the nature and dynamics of changes in the prevalence of bladder cancer among the population of Ukraine at the local levels for two five-year periods (2009-

2013 and 2014-2018), the general similarity in certain features is traced (Table 1). If we take into account the years of study, then additional comments to their original absolute values are not required.

The data in Table 1 show indicators of confirmation of the growth rate of patients with BC registered in each of the periods, with a less intensive process in the latter. Over 10 years, the prevalence rate increased by 21.7% to 79.5, according to absolute data – by 11.8% to 33,552 cases in 2018.

Table 1

Dynamics of bladder cancer prevalence among the adult population of Ukraine by periods of study

Years Values	I period		R g/d; %	II period		R g/d; %	R g/d; % from 2009 to 2018
	2009	2013		2014	2018		
Absolute values	30006	34511	15.0	30812	33552	8.9	11.8
Intensive coefficients (per 100 thousand of the corresponding population)	65.3	75.5	15.6	71.8	79.5	10.7	21.7

Note. $x/R_{g/d}$ – growth rate (decrease); %.

Importantly, the largest number of patients with BC is constantly concentrated in six virtually unchanged administrative territories (in five regions: Dnipropetrovsk, Donetsk, Lviv, Odessa, Kharkiv and the capital; in 2014-2018 Donetsk was replaced by Zaporizhzhia). In 2009 they accounted for 11062 cases, which was 36.9%, in 2013 – 15519 and 45.0%, in 2014 – 14783 and 46.5%, in 2018 – 15334 and 45.7% of the total. It is pertinent to note that 40.2%, 40.3%, 36.4% and 37.0% of the adult population of Ukraine lived in the listed territories, respectively. However, the results of comparing the number of registered patients and the population in the regions do not allow to identify a clear relationship between them, which indicates the existence of other factors influencing on the situation. The growth of the prevalence of BC in Ukraine as a whole, like the absolute values, is somewhat slower in 2014-2018 than in previous 2009-2013 – 10.7% vs. 15.6%. As a result, in 2018 the indicator was 79.5 against 71.8 in 2014 and 75.5 in 2013 against 65.3 in 2009 (per 100 thousand adult population). For convenience, only numerical values of indicators will be given in the text below. During the analysis of data in terms of oblasts, a noticeable feature was found. Each of the periods was characterized by almost the same composition with a level higher

than the average Ukrainian. And over the years it has expanded. In 2009 there were 9 of them, in 2013 – 12, which was 33.3% and 44.4% of their total number respectively; in 2014 – 12, in 2018 – 16 (48.0% and 64.0% respectively). In 2018, they included the following: Vinnytsia (91.0), Zaporizhzhia (106.1), Kyiv (91.8), Kirovohrad (106.0), Luhansk (92.4), Lviv (109.3), Mykolaiv (109.1), Odessa (119.2), Poltava (87.1), Sumy (87.6), Ternopil (82.3), Kharkiv (107.4), Kherson (87.5), Cherkasy (97.1), Chernivtsi (99.8) and Kyiv (89.7). The lowest prevalence levels were in Zakarpattia (40.7) and Rivne (43.9) oblasts out of 9, where the indicators were lower than the national average.

The above information in its comparative aspect confirms the independence of the number of patients with BC who are registered from the population in the administrative territories. The presence of certain changes, as can be predicted, is subject to the effectiveness of medical care and its organization. These issues become especially relevant. Over the years, in Ukraine patients have accumulated who constantly need different types of it. Moreover, with their total number, the number of incident patients is growing at the same time. Dynamics over the years is presented in Tables 2 and 3.

Table 2

Dynamics of bladder cancer incidence in adults in the first period (2009-2013) in Ukraine taking into account gender

Values	2009			2013			Growth rates (%)		
	total	including		total	including		total	men	women
		men	women		men	women			
Absolute values	4792	3910	882	5007	4051	956	4.5	3.6	8.4
Intensive coefficients (per 100 thousand of the corresponding population)	10.4	18.5	3.6	11.0	19.3	3.9	5.8	4.3	8.3

When evaluating the data in Tables 2 and 3, it is seen that the nature of changes in prevalence rates is preserved in its incidence. The increase in absolute and relative values is manifested at a lesser pace in the last five years (2014-2018). Namely: the former increased from 4792 to 5007 patients during 2009-2013, i.e. by 4.5%, and from 4251 to 4330 in 2014-2018 – 1.8%; incidence rates - from 10.4 to 11.0 by 5.8% and from 9.9 to 10.3 by 0.4%, respectively, among the adult population of both genders. The percentage of men exceeds that of women by more

than 4 times, in 2009 it was equal to 81.6%, in 2013 – 81.0%, in 2014 – 80.6%, in 2018 – 81.1%; levels were 18.5 and 19.3 and 17.3 and 18.0%, and their dynamics confirms the trend of growth retardation (by 4.3% and 4.0%). Another picture was observed among women. Their growth during 2009-2013, which was almost twice as high as for men (according to absolute data 8.4% vs. 3.6%, relative – 8.3% vs. 4.3%), stopped in the next five-year period - values remained at the same level.

Table 3

Dynamics of bladder cancer incidence in adults in the second period (2014-2018) in Ukraine taking into account gender

Values	2014			2018			Growth rates (%)		
	total	including		total	including		total	men	women
		men	women		men	women			
Absolute values	4251	3430	821	4330	3511	819	1.8	2.4	0.2
Intensive coefficients (per 100 thousand of the corresponding population)	9.9	17.3	3.6	10.3	18.0	3.6	4.0	4.0	0

Note that 24.6-35.7% of the total number of newly diagnosed patients with BC is concentrated in 5-6 administrative territories (Dnepropetrovsk, Donetsk, Lviv, Odessa, Kharkiv, Zaporizhia and Kyiv, the second oblast mentioned has been excluded from the list since 2014). They do not differ

from those identified in the analysis of the number of patients who are registered. The composition of oblasts where incidence rates exceed nation-wide indicators is almost identical, which does not require their list. We will note only that the highest (for example, in 2018 from 13,1 to 18,06 at averaged in

the country 10,3) they were in Vinnytsia, Zaporizhia, Kirovograd, Odessa, for all years and in the last year Kherson, Cherkasy, Chernihiv oblasts joined them. Zakarpattia (6.0) and Rivne (6.3) oblasts (2018) are distinguished by the lowest indicators. According to the dynamics of BC incidence rates of the male population, the number of oblasts with values higher than the national average is increasing, due to Mykolayiv, Sumy, Ternopil, and Cherkasy oblasts.

The defining criterion of medical care delivery is the detection of the disease in its early stages. However, the analysis of the relevant data shows a disappointing picture. Despite the increase in the number of oblasts in both periods (from 12 to 14 in 2009 and 2018, respectively) with a higher rate than nation-wide, over the years, unfortunately, the percentage of newly diagnosed BC patients with stages I-II decreases: from 84.21% in 2009 to 72.25% in 2013, as well as from 74.79% in 2014 to 72.22% in 2018. In addition, the number of cases with stages III-IV is growing: from 12.0% in 2009 to 23.83% in 2013 and from 21.67% in 2014 to 22.64% in 2018. At the same time the percentage of first diagnosed patients with stage IV increased – 8 areas in 2009, 12 – in 2018. We specify the data for 2018, when the average value of 7.91% in 12 administrative territories was exceeded: Vinnytsia (8.46), Dnepropetrovsk (12.62), Donetsk (12.32), Zhytomyr (8.46), Zakarpattia (30.16), Kyiv (11.56), Kirovohrad (9.62), Lviv (11.11), Odessa (10.58), Ternopil (8.57), Chernivtsi (10.45), Chernihiv (12.88). Under such conditions, the issue of early diagnosis of pathology remains problematic, which increases the need for search and implementation of modern methods and enhances the importance of simple and widely available organizational measures. They are primarily concerned with improving the means of public awareness with an increased emphasis on the importance of care and maintaining own health, which will lead to an increase in number of occupational medical check ups. Now there is low percentage of patients, which even decreases over the years. Thus, in the country: in 2014 – 18.0%, in 2018 – 16.9%, while in 2009-2013 it increased from 13.0% to 17.5%. In 7-9 oblasts the indicator exceeded the national average and among them Mykolayiv (26.7%-36.0%) and Rivne (41.8%-59.7%) are distinguished in terms of size; in Zakarpattia, Lviv, Ivano-Frankivsk the value is only in the range of 0.9-3.6%.

At the same time, due to research and involvement of modern methods of BC treatment used in clinical oncology, in Ukraine there is a positive dynamics of treatment effectiveness. The criteria for

such an assessment are the dynamics of the percentage of deaths up to one year from the time of diagnosis and those who are under supervision for 5 years or more. The second period looks better in this regard. Thus, the first indicator during 2014-2018 decreased from 15.6% to 14.7%, the second - increased from 56.5% to 59.1%. For comparison: in 2009-2013 their values (20.32% and 23.84%, respectively) confirmed the growth; and according to the second indicator – with their growth they were lesser (52.5% and 55.9% respectively). An important result of the comparative analysis of areas with higher than average percentages of patients detected during the professional examination, with the first diagnosis in stage I-II of the disease and those living under supervision ≥ 5 years, was the lack of the expected clear logical relationship in some cases. It is difficult to explain the traced data. The reason is the presence of regional features related, for example, to the composition of the population and its habits, mentality, way of life and attitude to it, etc. In addition, professionalism of specialists and the principles of organization of medical care are the essential factors.

Over the years, there has been a tendency to reduce the number of patients receiving special treatment in treatment and prevention facilities in Ukraine. If their percentage in 2009 was 17.0%, then in 2013 – 16.0%, in 2014 – 15.5%, in 2018 – 14.7%. The tendency still persists for those with the first registered BC, namely: 65%, 63.9%, 62.4%, 61.2%, respectively. In the second period, there are more oblasts where both of these parameters exceed the national average (in 2009-2013 there were 9 of them, while in 2014-2018 there were 15). Volyn, Zhytomyr, Ivano-Frankivsk, Kyiv, Khmelnytsky, Chernihiv, and Ternopil oblasts are distinguished on this basis. In the structure of types of treatment, surgery always ranked first, and its percentage was quite stable (37.8-40.0%). Almost 10 administrative territories had higher values of the indicator, among which the presence of specialized departments at higher medical institutions prevailed (Vinnytsia, Dnipropetrovsk, Donetsk, Zaporizhia, Zakarpattia, Lviv, Odessa, Kharkiv, Kyiv). Combined treatment ranked second: about a fifth of patients (19% and 21.2% in 2009 and 2013 and 17.9% and 19.2% in 2014, 2018 respectively). The other two – radiation and chemotherapy accounted for 3.4%, 2.3% and 2.8%, 1.4%, as well as 1.6%, 2.2% and 1.9%, 2, 6% respectively. That is, the use of radiation therapy is by 1.5 and 2 times less periods, while in range of chemotherapy is increasing in clinical practice. Chemotherapy does not exceed one percent. Of course, the study of data in terms of areas reveals the

frequency of the last three methods. In 3-4 oblasts the radiation method is absent or provided to 1-12 patients and only up to 25-30 people received it in Zhytomyr, Sumy, Ternopil. Chemotherapeutic method is more common (up to 11-12 cases) in Vinnytsia, Dnipropetrovsk, Zaporizhia. The internal distribution of frequency of these or those methods of treatment, i.e. in the section of areas is interesting. It turned out that in 2009, out of 2,039 cases of surgical treatment in 20 oblasts, it did not exceed 5% and ranged from 0.9% in Poltava to 4.5% in Vinnytsia; in the remaining 6 oblasts the percentage did not exceed 10% and was in the range of 6.1%-9.5% in Kyiv and Odesa oblasts, respectively. Important is the fact that, despite the change towards the spread of surgical methods in worldview, for 10 years no significant changes have taken place in the country. In 2018, out of 1867 surgical interventions, up to 5% again accounted for 20 oblasts (from 0.9% to 4.8% in Zakarpattia and Kyiv oblasts, respectively), and 10% in 6 oblasts (6.8%-9.3% in Zaporizhia and Lviv respectively).

Thus, having studied the dynamics of epidemiological processes, the effectiveness of specialized care for patients with BC over a 10-year period, we can confidently say about the unfavorable situation in Ukraine. There is an increase in the prevalence of pathology, which acquires its intensity over the years and is manifested by the accumulation of the number of patients. And although the growth rate was somewhat slower in 2014-2018, its high rates among the male population attract attention, as does the declining trend in the percentage of patients first detected in stages I-II and increase in III-IV, especially in the latter. At the same time, the effectiveness of the role of professional examinations remains low. Although advances in BC treatment have increased the proportion of those registered for 5 years or more, about 15% have died within a year of being diagnosed in the last five years. Over the years, the number of BC people treated for the first time is growing. In the structure of care delivery surgical, complex methods (up to 60%) dominate, radiation, chemotherapy and chemoradiation account for up to 5%. Peculiarities as for separate administrative territories are revealed. According to the results of the analysis, promising issues are highlighted. First of all, the expansion of opportunities for early detection of the disease, which include purely scientific developments and the use of new technologies, as well as various organizational, management measures, the composition of which is individually selected according to regional differences and features. The spread of modern principles of treatment of patients, which are

subordinated to the stage of the detected oncological process, also remains relevant.

CONCLUSIONS

1. There was revealed a steady increase in the incidence of bladder cancer in Ukraine with a slightly lower intensity in 2014-2018 against 2009-2013 (by 4.0% against 5.8%, respectively); in 2018 its level was 10.3 per 100 thousand of adults.

2. The disease incidence of BC in men prevails and increases over the years, but more slowly (by 4.0% against 4.3% in 2014-2018 and 2009-2013, respectively); as a result, in 2018 the figure was 18.0 against 17.3 in 2014 per 100 thousand of male population. Indicators among women increased intensively during 2009-2013 (by 8.3%) to 3.9 in 2013 and stabilized at 3.6 per 100 thousand female population in 2014-2018.

3. The accumulation of the number of BC patients in Ukraine has been established; in 2018, 33,552 cases were registered. The growth rate of absolute and relative values for 2009 - 2013 and 2014-2018 was 15.0%, 8.9% and 15.6%, 10.7%; for ten years 11.8% and 21.7% respectively. In 2018, the prevalence rate was 79.5 against 71.8 in 2014, 65.3 in 2009.

4. There has been revealed the peculiarity of the effectiveness of specialized care delivery to reduce the number of newly diagnosed patients during professional examinations (in 2018 – 16.9% against 18.0% in 2014), the percentage with a diagnosis established at stages I-II (72), 2% vs. 74.79%), while one in five has stage III-IV. In a tendency to increase the number of registered patients ≥ 5 years (59.1% vs. 56.5%), the death rate changed within a year from the time of diagnosis (14.7% vs. 15.6%, respectively).

5. Among the total number of those who received specialized care, up to 65% are newly diagnosed patients; in their structure, the surgical type accounted for 37-40% over the years, the combined treatment (up to 20% over the years) ranked second, followed by radiation and chemotherapy, which together did not exceed 5.0%.

6. There have been identified areas which are distinguished among others by large or low indicators for all the parameters studied, relative to the average Ukrainian ones. Their dependence on the population has not been revealed, as well as between the seemingly logically related indicators: the percentage of professional examinations, detected cases in stages I-II, III-IV, those who died within a year of diagnosis and those who are followed up for more than 5 years. In the presence of regional differences, there is a need for in-depth research on

this issue, including the quality and organization of care delivery.

Conflict of interest. The authors declare no conflict of interest.

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