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CLINICAL AND EPIDEMIOLOGICAL CHARACTERISTICS OF BONE SARCOMAS IN THE REPUBLIC OF KAZAKHSTAN IN 2010-2019

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ABSTRACT

Relevance: *Sarcomas are a heterogeneous group of mesenchymal origin malignant neoplasms (MNs). The peak incidence of bone tumors falls at a socially significant age: with osteosarcoma and Ewing's sarcoma – 10-25 years, with chondrosarcoma – 35-40 years. Bone sarcomas are the most aggressive human MNs. This urges to determine the prognostic factors of the disease, timely assess the treatment effect, and identify possible relapses.*

The study aimed to *improve the early diagnosis of bone sarcomas, to improve and increase the oncological alertness of doctors by establishing the trends in bone sarcoma incidence and mortality in Kazakhstan in 2010-2019 and this disease incidence and mortality in 2019 by age, gender, bone tumor histotype and region of the country.*

Materials and Methods: *This study included the data of all patients registered at the Electronic Registry of Oncological Patients (EROP) of the Republic of Kazakhstan in 2010-2019 with a "bone sarcoma" diagnosis (ICD-10 code: C40-C41). The incidence of bone sarcomas was presented as absolute and crude rates per 100,000 population. Absolute standardized morbidity and mortality were calculated using the World Standard. MS Excel 2016 was used to display the results graphically.*

Results: *By the end of 2019, 1587 patients were registered with bone sarcomas in Kazakhstan. From 2010 to 2019, the incidence of bone sarcoma in Kazakhstan decreased by 39%, including 36% among men and 40% among women. Mortality decreased by 37% to 0.7% per 100,000 population. Bone sarcoma is not among the 20 most common types of cancer in Kazakhstan. It accounts for 0.7% of all new cases of MN (2010-2019). The peak incidence of bone sarcoma was observed at the age below 20 years (20%), and mortality – was registered at 45-54 years (22%).*

Conclusion: *The rare occurrence of bone MNs can cause misdiagnosis during the initial examination. Bone sarcomas account for 0.8% of all MNs diagnosed in Kazakhstan. However, the aggressiveness of the course and rapid hematogenous metastasis causes a high percentage of neglect of this disease during the initial visit. In addition, bone sarcomas are more common than other MNs in young adults and adolescents. Therefore, the prognosis of primary bone sarcomas depends on many factors.*

Keywords: *epidemiology, morbidity, bone sarcomas, mortality.*

Introduction: Sarcomas are a heterogeneous group of malignant neoplasms (MNs). The peak incidence of bone tumors falls at a socially significant age: with osteosarcoma and Ewing's sarcoma – 10-25 years, with chondrosarcoma – 35-40 years. Bone sarcomas are the most aggressive human MNs. This urges to determine the prognostic factors of the disease, timely assess the treatment effect, and identify possible relapses [1]. In addition, population-based cancer registries rarely separate bone sarcomas into different histological types.

Bone sarcomas are sporadic neoplasms, making it difficult to determine the true incidence. It is also one of the main groups of rare cancers in Europe, accounting for about 1% of all diagnosed cancers [2, 3]. According to the World Health Organization, there are about 70 histotypes grouped into two main categories: soft tissue sarcoma and bone sarcoma [4]. In Europe, soft tissue sarcomas are more common than bone sarcomas, with global age-standardized rates (ASR) of 1.5-3.0/100,000/year and 0.5-2.0/100,000/year, respectively. Sarcomas are more common in men than in women [5]. In the United States, about 2,970 new cases of bone sarcoma were diagnosed in 2015, and about 1,490 patients died from the disease.

Malignant bone tumors tend to have a reasonably stable incidence at any age. However, a high incidence is reported in adolescents and young adults due to osteosarcoma and Ewing's sarcoma. A moderate increase in the incidence of bone tumors is also reported in people aged 70 to 80 years old.

In adolescents and children, osteosarcoma (56%) and Ewing's sarcoma (34%) are diagnosed much more often than chondrosarcoma (6%). Less than 5% of cases of chondrosarcoma and chordoma occur in this age group.

In adults, chondrosarcoma accounts for more than 40% of primary bone sarcomas. The mean age of incidence of this type of bone sarcoma is 51 years. Osteosarcoma is the next most common type of bone sarcoma in adults (28%) and is followed by chordoma (10%), Ew-

ing's sarcoma (8%), and fibrosarcoma (4%). Other types of bone sarcomas are rare.

Approximately 50% of bone sarcomas are diagnosed before 35 years. The second and third decades of life are the prominent peaks of incidence.

The study aimed to improve the early diagnosis of bone sarcomas, to improve and increase the oncological alertness of doctors by establishing the trends in bone sarcoma incidence and mortality in the Republic of Kazakhstan in 2010-2019 and this disease incidence and mortality in 2019 by age, gender, bone tumor histotype and region of the country.

Materials and Methods: This study included the data of all patients registered at the Electronic Oncological Patients (EROP) of the Republic of Kazakhstan in 2010-2019 with a "bone sarcoma" diagnosis (ICD-10 code: C40-C41). Information in EROP reflects demographics, disease stage, tumor histology, treatments, and survival data across the country. Demographic variables included gender, age, and regions of residence. The incidence of bone sarcomas was presented as absolute and crude rates per 100,000 population. Absolute standardized morbidity and mortality were calculated using the World Standard. MS Excel 2016 was used to display the results graphically [6].

Results: *Dynamics of bone sarcomas in the Republic of Kazakhstan in 2010-2019*

From 2010 to 2019, 2,272 cases of bone sarcoma were reported in Kazakhstan and averaged 0.8% per 100 thousand population. The incidence of primary bone sarcomas is higher in men than in women by 18%. The morbidity during the decade was 1,094 (48%) in men and 896 (42%) in women.

During the decade under study, high bone sarcoma incidence rates in Kazakhstan were observed in 2010 and 2014. In subsequent years (the last five years), there has been a decrease in bone sarcoma incidence by 37% since 2014 and 39% since 2010 (Fig.s 1). The incidence decreased among men by 36% and 40% among men and women, respectively (Fig.s 2, 3).

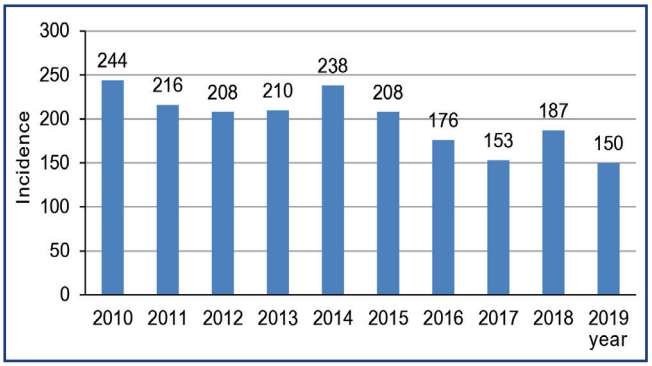

Figure 1 – Bone sarcoma incidence rates in 2010-2019 in Kazakhstan, both sexes (absolute prevalence)

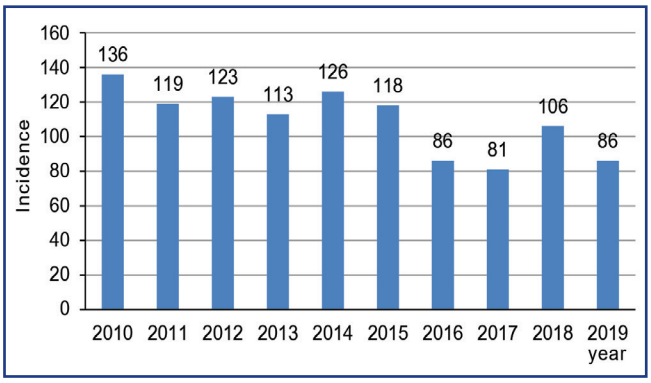

Figure 2 – Bone sarcoma incidence rates among men in 2010-2019 in Kazakhstan (absolute prevalence)

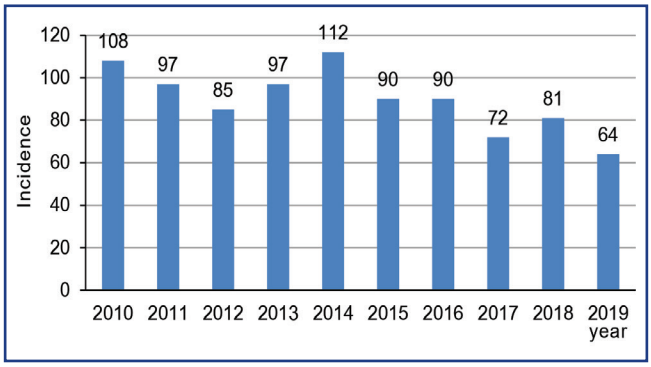

Figure 3 – Bone sarcoma incidence rates among women in 2010-2019 in Kazakhstan (absolute prevalence)

During the decade under study, bone sarcoma mortality in Kazakhstan also decreased by 37% and amounted to 0.7% per 100,000 population (Fig. 4).

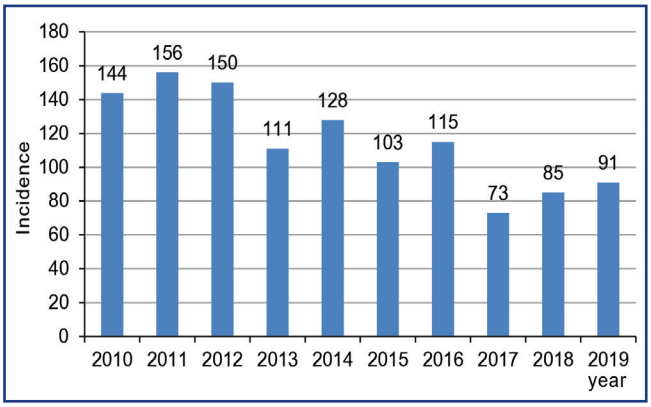

Figure 4 – Mortality rates of bone sarcomas 2010-2019 in Kazakhstan, both sexes (absolute prevalence)

The incidence reduced during the decade under study, but the mortality increased by 67% in 2011, 72% in 2012, 65% in 2016, and 60% in 2019. The annual mortality during the decade averaged 25.7% (Fig. 5).

In the study period, the number of patients with bone sarcomas registered at oncological organizations in Kazakhstan for more than five years has increased from 65.40% to 70%, with an average of 63.22%.

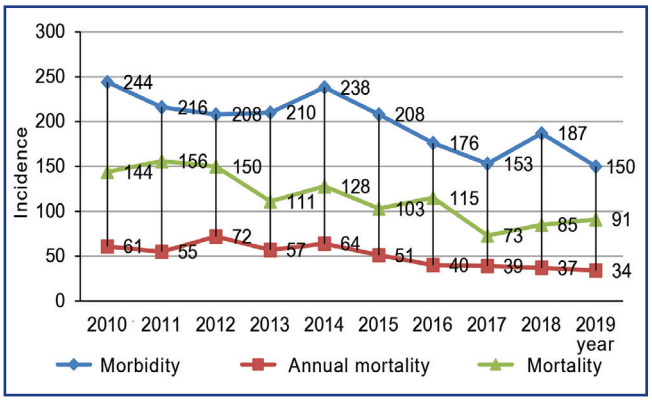

Figure 5 – Morbidity, mortality, and annual bone sarcoma mortality in 2010-2019 in Kazakhstan, both sexes (absolute prevalence)

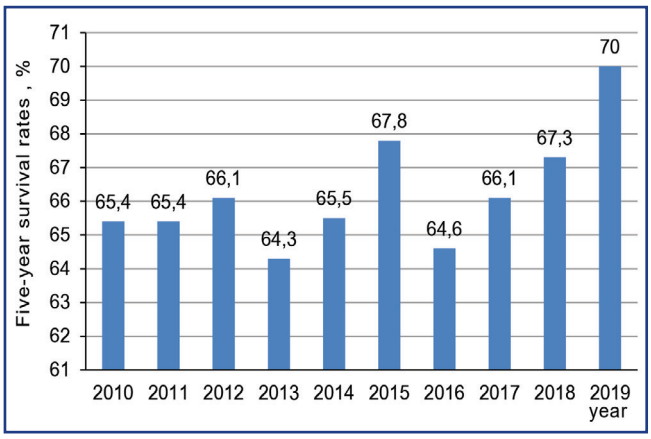

Figure 6 – Five-year survival rates of bone sarcomas in 2010-2019 in Kazakhstan, both sexes (%)

Epidemiological picture of bone sarcomas in the Republic of Kazakhstan, 2019

In 2019, 32,573 new cases of MN were registered in the Republic of Kazakhstan. Among them, 150 (0.5%) patients had bone sarcomas. In the structure of cancers, bone sarcomas occupied the 22nd place (0.8% per 100,000 population) (Fig.s 7.8).

In 2019, there were 14% more men (n=86) than women (n=58) among affected patients. The number of registered men and women with this diagnosis was 1.0% and 0.7% per 100 thousand of the population of the corresponding sex, respectively (Fig. 9).

Incidence peaks of bone sarcomas in 2019 were reported in young people aged 20-34 years (21%) and adolescents under 20 years (20%). At 45-74 years, bone sarcoma incidence amounted to 14-15% (Fig. 10).

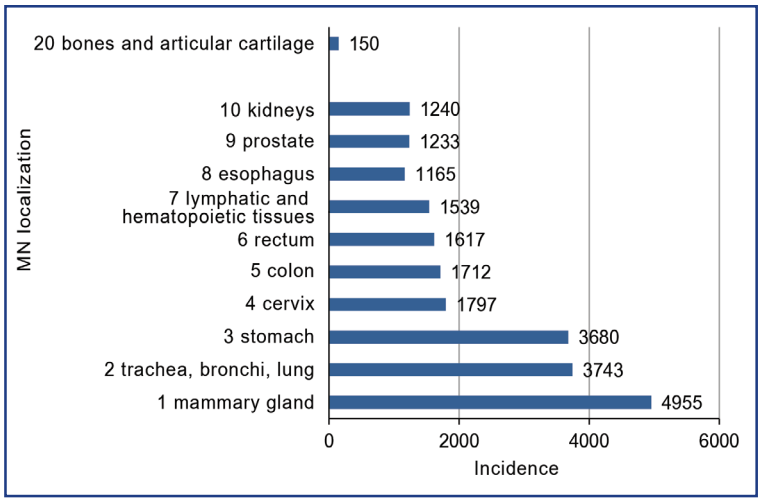

Figure 7 – Structure of cancers in Kazakhstan, 2019, both sexes (absolute prevalence)

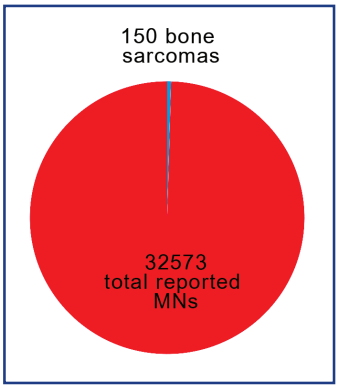

Figure 8 – Ratio of bone sarcomas to the total number of registered cancers in Kazakhstan in 2019 (absolute prevalence)

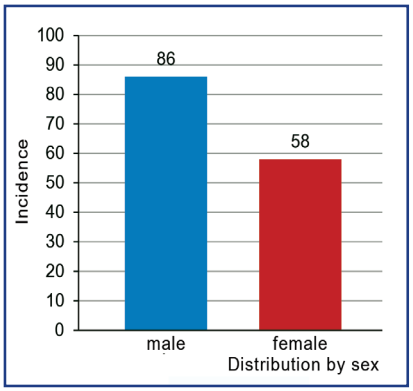

Figure 9 – Bone sarcoma incidence rates among men and women in Kazakhstan in 2019 (absolute prevalence)

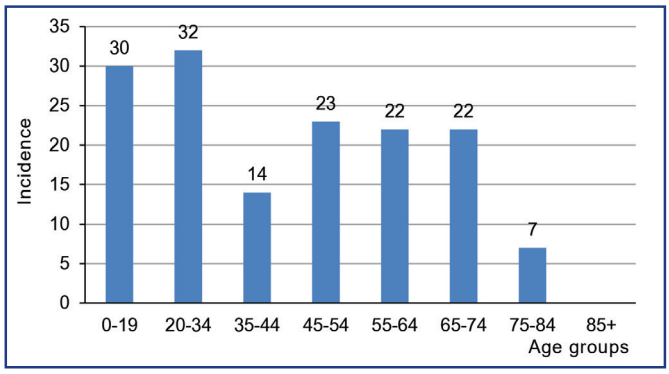

Figure 10 – Bone sarcoma incidence rates by age in Kazakhstan, 2019 (absolute prevalence)

The male incidence was 7-15% higher in almost all age groups, except for 35-44 years and over 75 years. The female incidence was 4% and 1% higher in the two last groups, respectively (Fig. 11). At 65-74 years, the incidence equaled in both sexes (11%).

The most significant number of patients was identified with the second stage of the disease (44%), the first stage (21%), the third stage (18%), and the fourth stage of bone sarcoma (17%) (Fig. 12). In addition, 17 patients with giant-cell tumors of the bone were not included in the staging groups since this tumor was not staged.

In 2019, the number of MN deaths in the Republic of Kazakhstan was 14,069, of which 91 (0.5%) were due to bone sarcomas. Bone sarcomas occupied 22nd place in the structure of causes of cancer mortality in both sexes, and the mortality rate was 0.5 per 100,000 population (Fig. 13).

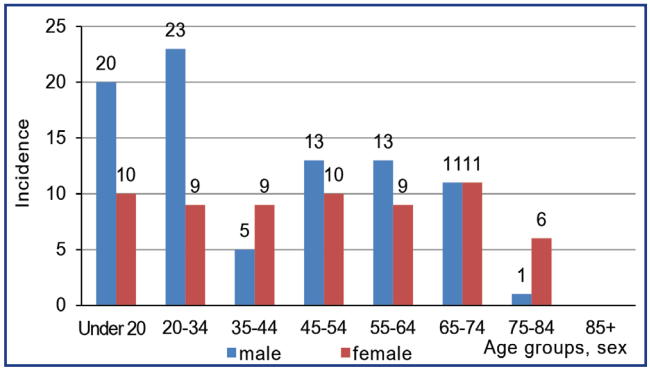

Figure 11 – Bone sarcoma incidence rates by age and sex in 2019 in Kazakhstan (absolute prevalence)

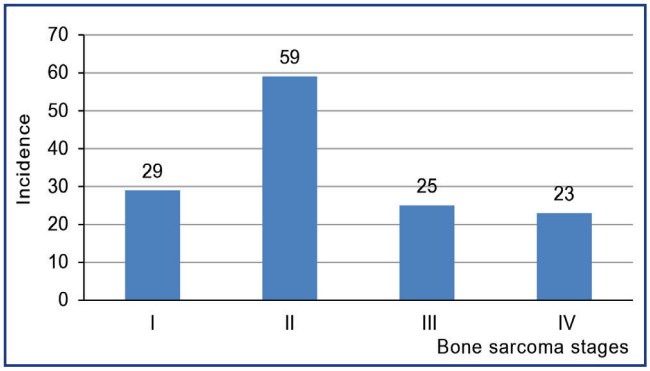

Figure 12 – Stage-specific bone sarcoma incidence rates in the Republic of Kazakhstan (absolute prevalence)

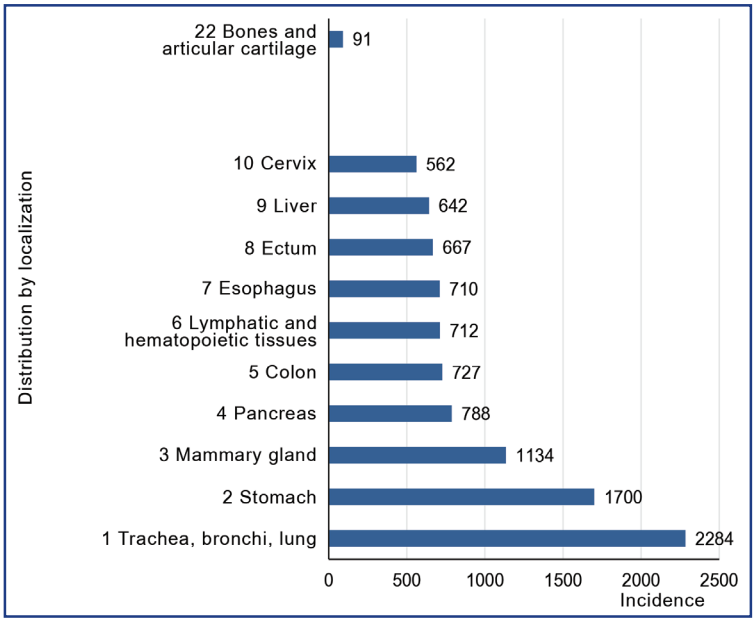

Figure 13 – Mortality rates of malignant neoplasms by localization in the Republic of Kazakhstan, 2019 (absolute prevalence)

Bone sarcoma mortality in 2019 in men was 43% higher (Fig. 14).

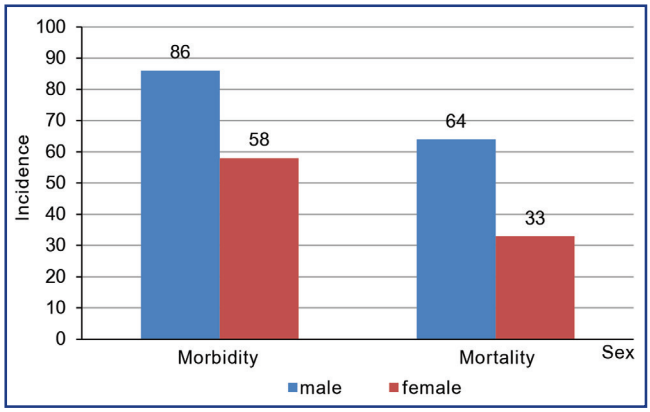

Figure 14 – Morbidity and mortality rates of bone sarcomas among men and women in the Republic of Kazakhstan in 2019 (absolute prevalence)

High mortality rates of bone sarcomas in 2019 were reported in the age group of 45-54 years (22%), 55-64 years (18%), and then those under 20 years (16%) (Fig. 15).

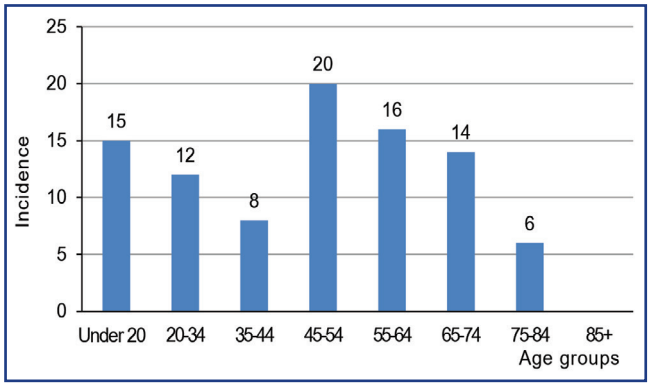

Figure 15 – Mortality rates of bone sarcomas by age in Kazakhstan in 2019 (absolute prevalence)

In all age groups, bone sarcoma mortality was higher in men. The peak was observed in groups of 45-54 years (13%), 55-64 years old (12%), and groups under 20 years and 20-34 years (11% each) (Fig. 19).

An increase in mortality was reported with decreased bone sarcoma incidence with increasing age in 2019 (Fig. 16).

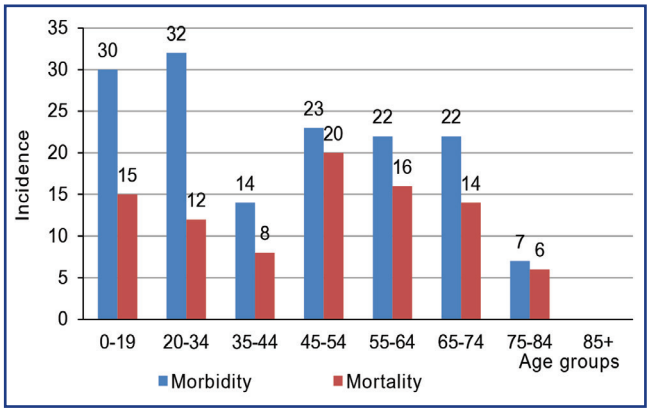

Figure 16 – Morbidity and mortality rates of bone sarcomas by age in the Republic of Kazakhstan in 2019 (absolute prevalence)

Among 150 cases of bone sarcomas diagnosed in 2019, 66% of osteosarcomas were reported in the age group under 20 years old, 39% cases were reported in the group of 20-34 years old, and 21% cases were reported in the 45-54 years old group. In 35-44 years, cartilaginous bone tumors were more common (35%). In the age group of 45-54 years, giant-cell tumor of the bone was diagnosed more often (35%) (Fig. 17).

The most common bone sarcoma in 2019 was osteosarcoma (33%), chondrosarcoma (16%), giant-cell tumor of the bone (11%), fibrosarcoma (7%), and the rarest bone sarcoma was Ewing's sarcoma (5%).

In 2019, bone sarcomas were most common in the long bones of the lower extremities (41%) and upper extremities (26%), as well as in the bones of the pelvis, sacrum, and coccyx (17%), ribs, sternum, and the collarbone (6%) (Fig. 18).

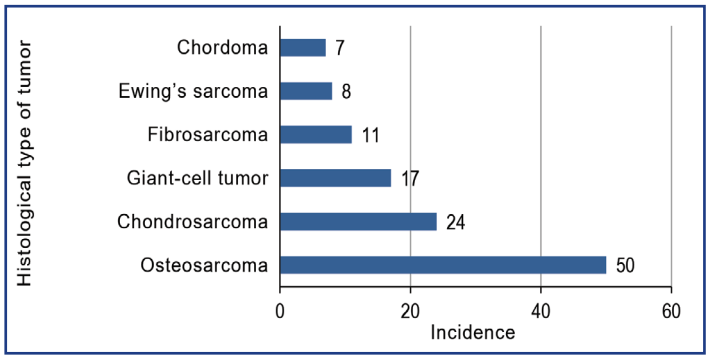

Figure 17 – Incidence rates of bone sarcoma by histological type in the Republic of Kazakhstan in 2019 (absolute prevalence)

In the Republic of Kazakhstan, the highest incidence of bone sarcomas in 2019 was reported in the Almaty region (18 cases; 12% of all cases registered during the year). Almaty was the second place (16 cases, 11%), and the Zhambyl region – the third (14 cases, 9%).

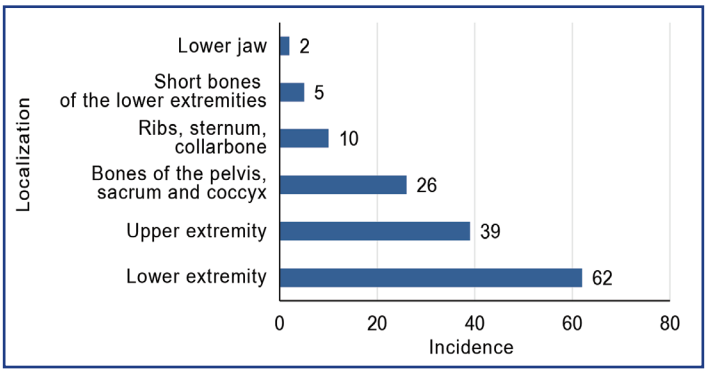

Figure 18 – Incidence rates of bone sarcoma by localization in the Republic of Kazakhstan in 2019 (absolute prevalence)

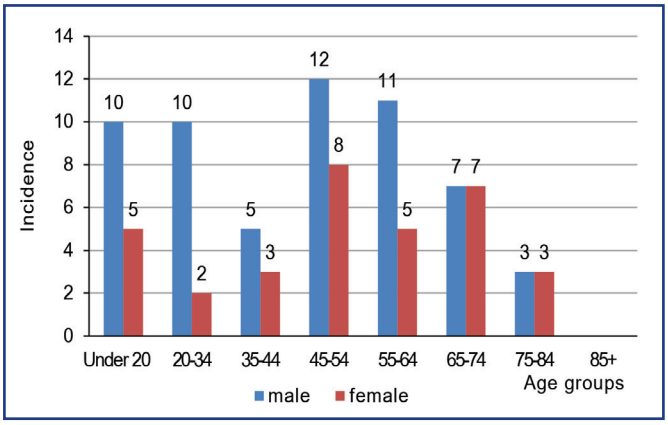

Figure 19 – Mortality rates of bone sarcomas among men and women by age in Kazakhstan in 2019 (absolute prevalence)

High mortality rates of bone sarcomas were found in Shymkent (10 cases, 11% of all deaths registered during the year), the East Kazakhstan region (9 cases, 10%), as well as in Almaty region and the city of Almaty (8 cases each, 9%) (Fig. 20).

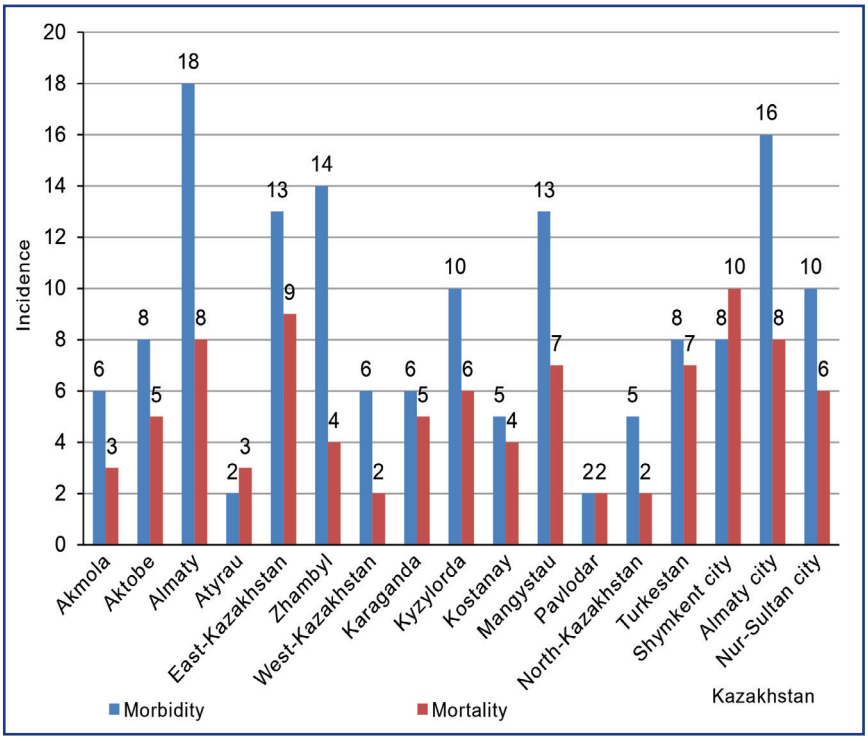

Figure 20 – Morbidity and mortality rates of bone sarcomas by region in Kazakhstan in 2019 (absolute prevalence)

In 2019, 1,587 cases of bone sarcoma were registered during the year, and 5.7% of them died from this disease. By the end of 2019, 1 113 (70% of all registered) patients had been registered at oncological organizations in Kazakhstan for more than five years.

One-year bone sarcoma mortality in 2019 was 23.2%. The ratio between one-year mortality and progression (stage IV at diagnosis) is 1.8%.

According to EROP of the RK, at the end of 2019, 70% of patients with bonne sarcomas had lived for more than five years since diagnosis.

Discussion: This article describes the statistics of bone sarcoma incidence and mortality in the Republic of Kazakhstan for the period from 2010 to 2019, as well as bone sarcoma incidence and mortality in 2019, depending on age, sex, histological type of tumor, localization, and regions of the Republic of Kazakhstan.

Over the decade (2010-2019), the population of Kazakhstan has increased. The bone sarcoma incidence has decreased, with an increase in mortality in 2011, 2012, 2016, and 2019. The average annual mortality increased up to 25.7%, indicating the existing challenges in timely diagnostics of bone sarcomas in the regions of Kazakhstan.

In 2019, among patients with MN of the bones, the largest group included patients with osteosarcoma, particularly those under 34 years. Further, with increasing age, more cartilage and giant-cell tumor of the bone are reported, while there is an overall decrease in incidence and survival rates. Bone sarcoma incidence among men is higher in almost all age groups, except for the average age of 35-44 years and over 75 years, where the incidence is higher in women. The onset of the disease is usually associated with a previous injury, which is more typical for young people and men.

In 2019, bone sarcomas occurred predominantly in the long bones of the lower extremities, less in the upper extremities and bones of the pelvis, sacrum, and coccyx, which corresponded to the morphological distribution of sarcomas (osteosarcoma, chondrosarcoma, giant-cell tumor of the bone, fibrosarcoma, and Ewing's sarcoma).

In 2019, the highest incidence of bone sarcomas was registered in the Almaty and Zhambyl regions. With a low incidence rate, bone sarcoma mortality was the highest in Shymkent, followed by the East Kazakhstan region and the city of Almaty. The highest bone sarcoma mortality in Kazakhstan was observed at 45-54 years.

It should be noted that the high ratio between one-year mortality and progression (stage IV at diagnosis) (1.8%) was reported, which indicates an underestimation of the prevalence of the disease and diagnostic errors. Therefore, the stage I and II bone sarcoma incidence rates in 2019 were overestimated.

Conclusion: Primary bone tumors are relatively rare but represent a significant problem. Occurring at any age, they most often affect children, adolescents, and young people and are prone to hematogenous metastasis.

The analysis of the statistics of bone sarcoma morbidity and mortality for ten years and more detailed analysis for 2019 indicate the difficulties in diagnosing this group of sarcomas, which requires the complex use of clinical, radiological, and morphological research methods.

Early and timely recognition of bone sarcomas, rational treatment tactics, and dynamic dispensary monitoring is of great importance in the prognosis of this disease.

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ТҰЖЫРЫМ

2010-2019 ЖЫЛДАРЫ ҚАЗАҚСТАН РЕСПУБЛИКАСЫНДАҒЫ СҮЙЕКТЕР САРКОМАСЫНЫҢ КЛИНИКАЛЫҚ-ЭПИДЕМИОЛОГИЯЛЫҚ СИПАТТАМАСЫ

Д.А. Тулеуова[1], Г.А. Серикбаев[1], А.К. Курманалиев[1], Ж.У. Пысанова[1], А.М. Елекбаев[1]

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Өзектілігі: *Саркомалар – мезенхималық шыққан қатерлі ісіктердің (МН) гетерогенді тобы. Сүйек ісіктерінің ең жоғары жиілігі әлеуметтік маңызды жасқа келеді: остеосаркома және Юинг саркомасы кезінде – 10-25 жас, хондросаркомамен – 35-40 жас. Сүйек*

саркомалары адамның ең агрессивті қатерлі ісіктері болып табылады. Осыған байланысты аурудың болжамды факторларын анықтау, емнің әсерін уақтылы бағалау және ықтимал қайталануларды анықтау қажет.

***Зерттеудің мақсаты** – сүйек саркомасының ерте диагностикасын жақсарту, 2010-2019 жылдар кезеңінде Қазақстан Республикасында сүйек саркомасымен сырқаттану және одан болатын өлім-жітім жиілігін, сондай-ақ жас топтарына, жынысына, сүйек ісіктерінің гистопиттеріне және елдің өңірлеріне байланысты 2019 жылы сырқаттану және өлім-жітім көрсеткіштерін зерделеу арқылы дәрігерлердің онкологиялық сақтығын жақсарту және арттыру.*

***Әдістері:** Зерттеу үшін 2010-2019 жылдар аралығында Қазақстан Республикасының Ұлттық онкологиялық реестрде тіркелген пациенттердің деректері пайдаланылды. сүйек саркомасы диагнозы қойылған (ICD-10 коды: C40-C41). Сүйек саркомасының жиілігі 100 000 халыққа шаққанда абсолютті және шикі көрсеткіштер ретінде ұсынылған. Абсолютті стандартталған аурушаңдық пен өлім-жітім көрсеткіштері Дүниежүзілік стандарттың көмегімен есептеледі. Нәтижелерді графикалық түрде көрсету үшін MS Excel 2016 пайдаланылды.*

***Нәтижесі:** 2019 жылдың қорытындысы бойынша ҚР сүйек саркомасы диагнозымен 1587 науқас тіркелді. 2010 жылдан 2019 жылға дейін ҚР сүйек саркомасымен сырқаттанушылық 39%-ға, оның ішінде ерлер арасында 36%-ға, әйелдер арасында 40%-ға төмендеді. Өлім-жітім 100 000 халыққа шаққанда 37%-ға, 0,8%-ға төмендеді. Сүйек саркомасы ҚР қатерлі ісіктің 20 кең тараған түрлерінің қатарына кірмейді, ол барлық жаңа МН жағдайларының 0,7%-ын құрайды (2010-2019). Сүйек саркомасының ең жоғары жиілігі 20 жаста (20%), ал өлім 45-54 жаста (22%) байқалды.*

***Қорытынды:** Сүйектердің МН сирек кездесетіні дәрігерге алғашқы бару кезінде диагноз қоюда қателік тудыруы мүмкін. Сүйек саркомасы Қазақстан Республикасында анықталған барлық МН-ның 0,8% құрайды, алайда ағымның агрессивтілігі және гематогенді метастаздың жылдам болуы бастапқы тексеру кезінде бұл ауруды елемеудің жоғары пайызын тудырады. Сонымен қатар, сүйек саркомасы жас ересектер мен жасөспірімдерде басқа МН-ге қарағанда жиі кездеседі. Бастапқы сүйек саркомасының болжамы көптеген факторларға байланысты.*

***Түйінді сөздер:** эпидемиология, аурушаңдық, сүйек саркомасы, өлім.*

АННОТАЦИЯ

КЛИНИКО-ЭПИДЕМИОЛОГИЧЕСКАЯ ХАРАКТЕРИСТИКА САРКОМ КОСТЕЙ В РЕСПУБЛИКЕ КАЗАХСТАН В 2010-2019 гг.

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***Актуальность:** Саркомы являются гетерогенной группой злокачественных новообразований (ЗНО) мезенхимального происхождения. Пик заболеваемости костными опухолями приходится на социально значимый возраст: при остеосаркоме и саркоме Юинга – 10-25 лет, при хондросаркоме – 35-40 лет. Саркомы костей являются наиболее агрессивными злокачественными опухолями человека.*

***Цель исследования** – улучшить раннюю диагностику сарком костей, улучшить и повысить онконастороженность врачей путем изучения частоты заболеваемости и смертности от сарком костей в Республике Казахстан за период с 2010 по 2019 годы, а также показателей заболеваемости и смертности в 2019 году в зависимости от возрастных групп, половой принадлежности, гистопитов опухолей костей и регионов страны.*

***Методы:** Для исследования были использованы данные пациентов, зарегистрированных в ИС Электронный регистр онкологических больных (ЭРОБ) РК с 2010 по 2019 гг. с диагнозом «саркома костей» (код ICD-10: C40-C41). Количество случаев сарком костей представлено в виде абсолютных и грубых показателей на 100 000 населения. Абсолютные стандартизованные показатели заболеваемости и смертности рассчитаны с применением мирового стандарта (World). Для графического отображения результатов использована программа MS Excel 2016.*

***Результаты:** На конец 2019 г. на учете с диагнозом «саркома костей» в РК состояли 1587 пациентов. С 2010 по 2019 гг. заболеваемость саркомой костей в РК снизилась на 39%, в том числе на 36% среди мужчин и на 40% среди женщин. Смертность снизилась на 37% до 0,8% на 100 тыс. населения. Саркома костей не входит в число 20 наиболее распространенных видов рака в РК, на нее приходится 0,8% всех новых случаев ЗНО (2010-2019 гг.). Пик заболеваемости саркомой костей отмечался в возрасте до 20 лет (20%), а смертности – в возрасте 45-54 года (22%).*

***Заключение:** Редкая встречаемость ЗНО костей может стать причиной ошибки в постановке диагноза при первичном обращении к врачу. Саркомы костей составляют 0,5% от всех ЗНО, выявленных в РК, но характеризуются агрессивностью течения и быстрым гематогенным метастазированием, что обуславливает высокий процент запущенности при первичном обращении. Помимо того, саркомы костей чаще других ЗНО встречаются у молодых людей и подростков. Прогноз первичных сарком костей зависит от многих факторов.*

***Ключевые слова:** эпидемиология, заболеваемость, саркома костей, смертность.*

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