EJMO

DOI: 10.14744/ejmo.2024.73478
EJMO 2024;8(2):194–198

Research Article

Epidemiology and Management of Hepatocellular Carcinoma in Kazakhstan

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Abstract

Objectives: Hepatocellular carcinoma (HCC) is the most prevalent primary liver malignancy, ranking sixth among all cancers and accounting for 95% of hepatobiliary tumors. The highest incidence rates are in Eastern Asia, Northern Africa, and South-Eastern Asia. In Kazakhstan, HCC is a significant public health issue due to its increasing incidence and high mortality rates.

Methods: This study analyzed data from 7072 HCC patients in Kazakhstan from 2012 to 2021, using the "Electronic Registers of Patients" covering 97% of the population. The study assessed age-, gender-, and ethnicity-specific incidence rates and compared regions using direct standardization.

Results: The incidence rate of HCC increased from 0.06 to 6.6 per 100,000 population over the study period ($R^2 = 0.8261$, p=0.001). Higher rates were observed in older individuals, males, and Europeans compared to Asians. Geographic disparities showed higher rates in West Kazakhstan and major cities (Almaty, Astana, Shymkent). Survival rates were low, with 1-year, 5-year, and 10-year survival at 37.7%, 12.5%, and 10.9%, respectively. Central Kazakhstan, particularly the Karagandy region, had better survival rates.

Conclusion: The study illustrates the rising incidence and poor survival of HCC in Kazakhstan, with significant demographic and geographic disparities.

Keywords: Hepatocellular carcinoma, Kazakhstan, incidence rate

Cite This Article: *Serikuly Y, Nurbakhyt A, Kaniyev S, Baimakhanov Z, Kanushina M, Doskhanov M, et al. Epidemiology and Management of Hepatocellular Carcinoma in Kazakhstan. EJMO 2024;8(2):194–198.*

Hepatocellular carcinoma (HCC) is the most common form of primary malignant neoplasm of the liver.[1] It ranks sixth among all registered cancer cases and accounts for 95% of tumors of the hepatobiliary system.[2] The incidence rates are particularly high in regions like Eastern Asia, Northern Africa, and South-Eastern Asia, indicating a significant geographical variance in HCC prevalence.[3] The Hepatitis B virus (HBV) is the primary cause of liver cancer cases and related deaths globally, accounting for 33%. This is followed by alcohol, which contributes to 30% of cases, the Hepatitis C virus (HCV) at 21%, and other factors making up 16%.[4] In Kazakhstan, HCC represents a particularly urgent public health issue, due to increasing incidence and the high mortality rates associated with the disease.

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Submitted Date: April 14, 2024 **Revision Date:** May 20, 2024 **Accepted Date:** May 23, 2024 **Available Online Date:** July 10, 2024

Early diagnosis of HCC is very important to prevent complications. Novel imaging equipment and non-invasive biomarkers shows favorable results.[5] Kazakhstan faces multiple challenges in diagnosis due to limited access to advanced imaging techniques and biomarker testing facilities. This also could contribute to future patients mortality and morbidity rate.

Kazakhstan has used various modalities of treatment, including surgical resection, liver transplantation, and locoregional therapies like radiofrequency ablation and transarterial chemoembolization. However, there is no available data about these burdens. This study aims to evaluate the current epidemiological trends of HCC, diagnostic modalities and assess the effectiveness of the existing treatment strategies in Kazakhstan.

Methods

We conducted a comprehensive analysis of all adult patients diagnosed with HCC in the Republic of Kazakhstan (RK) over the past ten years, from 2012 to 2021. The assessment of HCC incidence was based on data from the "Electronic Registers of Patients," a population-based disease registry covering 97% of all patients whole RK. The study protocol received approval from the Institutional Review Board, ensuring compliance with ethical standards for research involving human participants. The ethnic groups included the following: Asian, European. This system collected information on patient demographics, treatment modalities, and survival rates. Our analysis encompassed all regions of RK and significant cities (Almaty, Astana, Shymkent).

We calculated age-, gender-, and ethnicity-specific incidence rates (per 100,000 population) for each region and the three major cities. To compare data between regions, we employed the method of direct standardization, taking into account the population structure of each region and its changes over time. The survival rate was also calculated based on treatment type.

Incidence rates were calculated per 100,000 population, with trends over time analyzed using the R-squared (R^2) statistic and p-values to assess significance. Survival analysis was conducted using Kaplan-Meier curves, and differences between groups were tested using the log-rank test.

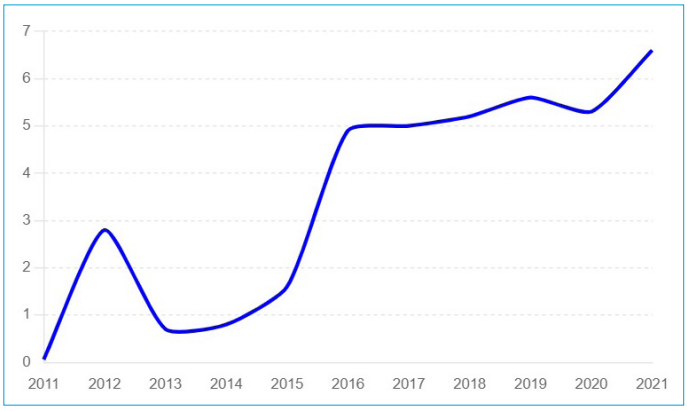

Figure 1. Mean annual standardized HCC incidence rates in the Republic of Kazakhstan, per 100000 population.

Results

7072 patients with HCC were registered from January 2012 to December 2021. The overall HCC in Incidence rate increased from 0.06 to 6.6 cases per 100,000 population from 2012 to 2022 (R^2 = 0.8261, p=0.001), which is indicative of an upward trend during the period under review as shown in Figure 1 (Table 1).

The patient demographic consisted of 52.9% women and 47.02% men, with an average age of approximately 65.2 years, indicating no significant age difference between

Table 1. Incidence Rates of Hepatocellular Carcinoma in Kazakhstan (2011-2021)

Years	Incidence rate
2012	2.8
2013	0.7
2014	0.8
2015	1.6
2016	4.9
2017	5.0
2018	5.2
2019	5.6
2020	5.3
2021	6.6

Table 2. Incidence Rates of Hepatocellular Carcinoma by Age Group, Gender, and Ethnicity

	Incidence rate	
Age group		
20 – 30	0.2	p>0.05
31 – 40	0.7	
41 – 50	2.9	
51 – 60	8.4	
61 – 70	22.5	
71 – 80	22.1	
Gender		
Male	4.3	ns
Female	2.9	
Ethnics		
European	3.7	ns
Asian	2.9	

genders. The incidence rate for males stands at 4.3 per 100,000 population, whereas for females, it is lower at 2.9 per 100,000 population (Table 2).

Individuals of European ethnicity have a higher incidence rate compared to those of Asian ethnicity. The incidence rate of HCC increases with age, peaking in the 61-70 age group, followed closely by the 71-80 age group. The rates are significantly lower in younger age groups (Fig. 2).

During all period of time there was observed gradually incresing of incidence throughout the country. Figure 3 shows the geographic distribution of HCC incidence rates in RK. The high incidence rate among regions showed the West Kazakhstan region 4,2 cases per 100 000 population. HCC also revealed the high rate than other regions in 3 cities of Republican significance Almaty, Astana and Shymkent 7,9; 10,4; 12,0 correspondingly. Almaty, Turkestan and Akmola oblasts demonstrated the lowest indication (1,0; 0,9; 1,0).

5-year overall survival illustrated very poor survival in RK, 1-year, 5-year and 10-year survival were 37.7%, 12.5%, 10.9% respectively (Fig. 4a). According to separate areas, central Kazakhstan has higher survival compared to west, north, south and east areas of Kazakhstan and there was found significant difference between groups (Fig. 4b). 10-year survival reached the number of 15.5% in central, the second area was the south, third was the west 5.9, and 4.4%, 4.3% the east and the north Kazakhstan areas. Karagandy region revealed significantly higher survival in comparison with all other regions (1-, 3- 5-year survival 60,0%, 37,5%, 33,0% respectively) (Fig. 4c).

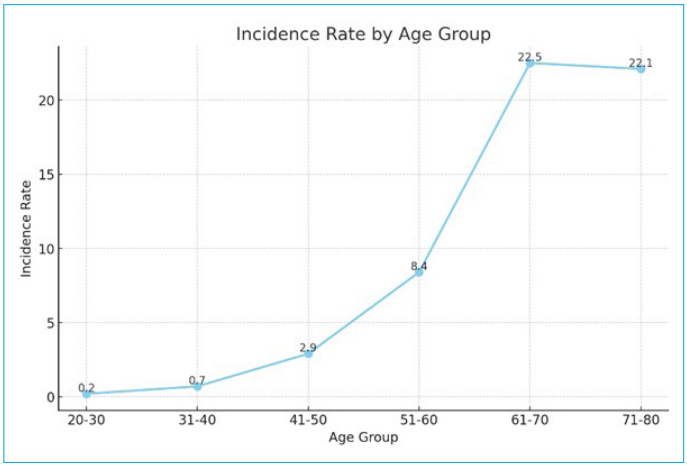

Figure 2. Hepatocellular carcinoma incidence rate by age group.

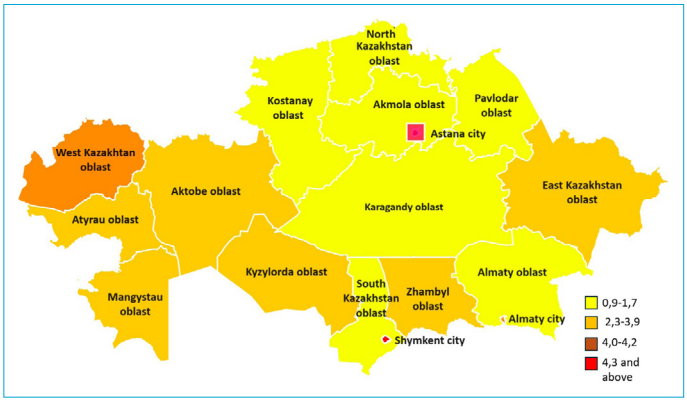

Figure 3. Hepatocellular carcinoma incidence rate in different Kazakhstan regions.

Discussion

Hepatocellular carcinoma remains a significant worldwide malignancy and is the third leading cause of cancer-related death.[6] HCC occupies a high position in morbidity and mortality among all types of cancer, and its incidence rate has increased significantly over the period under review.[7] HCC accounts for 4.2% of the total mortality from cancer,

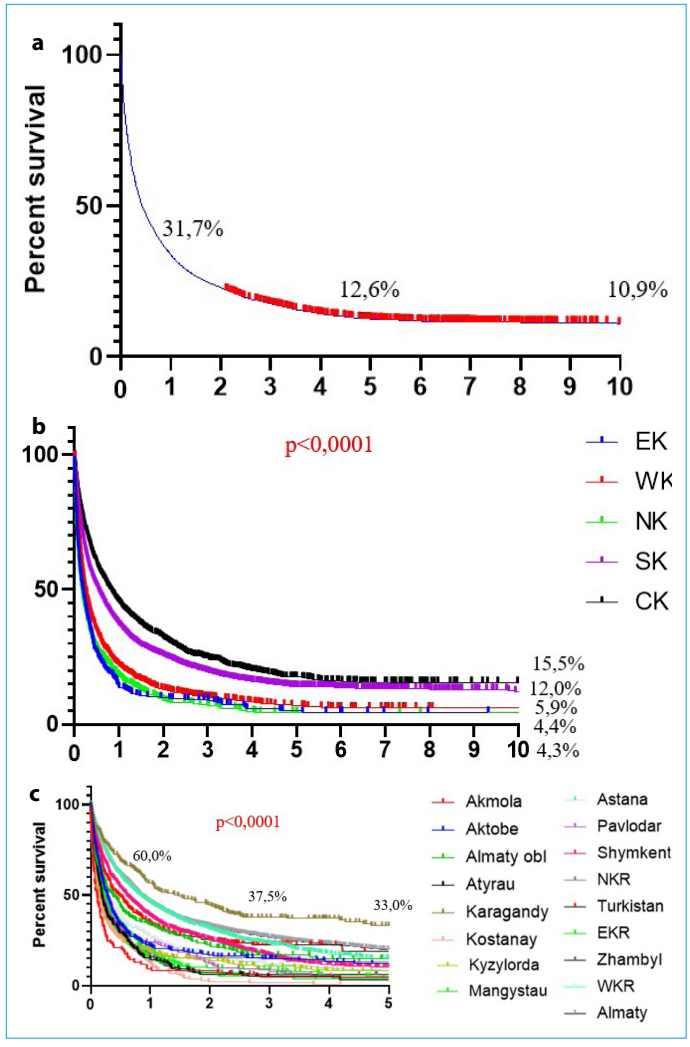

Figure 4. Overall survival rate of patients with hepatocellular carcinoma in **(a)** The Republic of Kazakhstan; **(b)** different areas (east, west, north, south, central); **(c)** different regions.

and the five-year relative survival rate for HCC is only 14%.[8] The findings of this study highlight several critical points regarding the epidemiology, diagnosis, and treatment of hepatocellular carcinoma (HCC) in Kazakhstan over the past decade. The marked increase in HCC incidence from 2012 to 2021 ($R^2 = 0.8261$, p=0.001) underscores the growing burden of this disease. The geographical variance, with the highest incidence in West Kazakhstan and major cities, suggests regional disparities possibly linked to environmental, genetic, or healthcare access factors.

In the gender aspect, it was also found that, in general, men have a higher incidence of HCC compared to women, which corresponds to international research data.[9] The analysis of gender-specific incidence rates of hepatocellular carcinoma (HCC) in Kazakhstan reveals a noticeable difference between males and females. The incidence rate for males stands at 4.3 per 100,000 population, whereas for females, it is lower at 2.9 per 100,000 population. Despite this difference, the p-value greater than 0.05 suggests that the variation in incidence rates between genders is not statistically significant.

The data indicates a higher HCC incidence among individuals of European ethnicity compared to Asian ethnicity within Kazakhstan. This discrepancy may point to underlying genetic susceptibilities or lifestyle differences that warrant further investigation. The significant role of HBV, alcohol, and HCV in HCC etiology, as seen globally, is likely mirrored in Kazakhstan, showing the need for targeted prevention and early detection strategies, particularly in high-risk groups.

The diagnostic challenges in Kazakhstan, such as limited access to advanced imaging and biomarker testing, likely contribute to delayed diagnoses and poorer outcomes. This gap in diagnostic capabilities is a critical area for healthcare policy intervention to improve early detection and management of HCC.

Comparing the Asian ethnic group with the European one, it should be noted that the Asian group has a higher incidence of genetically controlled HCC diseases by 3.4 times.[10] Survival analysis reveals a bleak prognosis for HCC patients in Kazakhstan, with 5-year survival rates at 12.5%. This poor survival rate may be attributed to late-stage diagnoses, suboptimal treatment modalities, and possibly inadequate follow-up care. Interestingly, central Kazakhstan, particularly the Karagandy region, demonstrated significantly better survival rates, which could be due to better healthcare infrastructure or more effective treatment protocols in that area.

The study's comprehensive approach, using a population-based disease registry, provides a robust dataset for understanding HCC trends. However, it also shows the need for improved data collection and reporting mechanisms across all regions to ensure a more accurate epidemiological picture.

Limitations include data quality, geographic disparities, limited diagnostic tools, potential confounding factors, and changes over time, suggesting cautious interpretation and the need for improved healthcare infrastructure and targeted prevention programs.

Conclusion

This study reveals the urgent need for enhanced diagnostic and treatment capabilities for HCC in Kazakhstan. Addressing these gaps through improved healthcare infrastructure, targeted prevention programs, and equitable access to advanced diagnostic and treatment options could significantly impact HCC outcomes. Future research should focus on the underlying causes of regional and ethnic disparities in HCC incidence and outcomes, as well as the effectiveness of different treatment modalities in Kazakhstan.

Disclosures

Ethics Committee Approval: The study was approved by Asfendiyarov Kazakh National Medical University Ethics Committee in 15.10.2021 №7.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – Y.S., B.B.; Design – A.S., A.B.; Supervision – B.B., Z.B., S.K., A.N., M.K.; Materials – A.S., D.M.; Data collection &/or processing – S.T., A.I., Z.O.; Analysis and/or interpretation – Y.S., A.B.; Literature search – Z.B., A.B., Z.O.; Writing – Y.S., A.B.; Critical review – S.K., Z.B., B.B.

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