STUDY OF PROSTATE CANCER PREVALENCE IN KAZAKHSTAN

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Received 08 Oct 2020, Accepted 17 Nov 2020

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ABSTRACT

Introduction. Prostate cancer is the second leading cause of cancer death worldwide, including developed countries. There are epidemiological studies on the prevalence of this disease in Central Asia. However, a study about the prevalence of prostate cancer depending on ethnicity in Kazakhstan was not conducted yet.

Objective. To assess the incidence rates of prostate cancer in relation to ethnicity, age and morphological type of tumour (in Kazakhstan).

Methods. This is a retrospective study of morphologically verified cases of prostate cancer, performed on 7082 patients during the period 2015-2019. According to ethnicity, the patients were subdivided into the following groups: Central Asians, Slavs, and other nationalities. Four categories were identified by age: <60 yo, 60-69 yo, 70-79 yo and 80+ yo. The information on the age difference, social status, stages of the malignant process, morphological type of cancer was collected.

RéSUMÉ

Introduction. Le cancer de la prostate est la deuxième cause de décès par cancer dans le monde, y compris les pays développés. Il existe un certain nombre d’études épidémiologiques sur la prévalence de cette maladie en Asie centrale. Cependant, la prévalence du cancer de la prostate en fonction de l’origine ethnique au Kazakhstan n’a pas encore été réalisée.

Objectif. Évaluer les taux d’incidence du cancer de la prostate par rapport à l’origine ethnique, à l’âge et au type morphologique de tumeur (au Kazakhstan).

Méthodes. Il s’agit d’une étude rétrospective de cas de cancer de la prostate vérifiés morphologiquement, réalisée sur 7082 patients couvrant la période 2015-2019. Selon l’appartenance ethnique, les patients ont été subdivisés dans les groupes suivants: Asiatiques
and analysed. The age-standardized incidence rate of prostate cancer was calculated depending on ethnicity. All statistical calculations were performed using SPSS software (version 22.0, IBM SPSS Inc., Chicago, Illinois, USA). A p value < 0.05 was considered statistically significant.

Results. The mean age of the patients was 69.04±8.5 years. Among 7082 patients, 61.6% were Slavs, 35.01% Central Asians and 3.37% other ethnic groups. Prostate cancer prevailed in the age group 60-69 yo in 41.9% cases, which was higher among Slavs compared to the Central Asians (p≤0.05). The average annual increase in the disease incidence was 2.1%. There was no significant increase in the incidence of prostate cancer in the age groups: <40 yo (r = 0.41), 40-49 yo (r = 0.31), +80 yo (r = 0.32). Stage II of the tumour process was the most diagnosed in the total number of cases (N = 2856), the highest prevalence being found among Slavs (40.66%) (p ≤ 0.05). Adenocarcinoma was the most frequently detected type of tumour (97.37%) in all ethnic groups.

Conclusions. The results of the study showed there was a relatively low increase in the incidence of prostate cancer in the Kazakhstan population between 2015-2019. A high incidence of prostate cancer among men of Slavic nationality than among Central Asians was determined. These findings indicate the importance of the early diagnosis of prostate cancer, especially in ethnic groups with a higher incidence of the disease.

Keywords: prostate cancer, ethnicity, incidence, mortality, cancer stage.

Abbreviations
ASR = The age-standardized incidence rate
NPCR = National Cancer Registry Program
GLOBOCAN = Global Burden of Cancer Study
ICD-10 = International Classification of Diseases
PSA = Prostate-specific antigen
PHI = Prostate Health Index

Introduction

Prostate cancer is the most common malignant tumour in men and the second leading cause of cancer death in developed countries. The risk of prostate cancer increases significantly as men get older. Despite the recent decline in the overall mortality rate from prostate cancer in all racial and ethnic groups, racial differences in mortality from cancer still persist.

In fact, there are significant differences in the incidence and prevalence of prostate cancer among members of different races and ethnic groups. According to GLOBOCAN data (2012), the highest incidence rates associated with prostate cancer worldwide were detected in the countries of Oceania, the United States, Europe and Africa, while Asia was the continent with the lowest incidence (except for West Asia). Apart from Africa, where the highest mortality was recorded, the mortality rate was fully consistent with the incidence rate in other countries.

Undoubtedly, the lack of systematic screening for prostate cancer in Asian countries can explain the low rate of incidence, but it cannot fully explain...
the low incidence risk among Asian immigrants in the United States and Western European countries. Another factor that can play a role in such a situation is the reverse immigration of older Asian immigrants to homeland8.

According to the available data, the incidence rates among various nationalities living in Central Asia have not been assessed yet6. Statistics reveals that the ethnic composition of the Central Asian countries such as Kazakhstan and Kyrgyzstan is very similar10,11. In this regard, the results of a study carried out in multinational Kazakhstan (130 nationalities) can be extrapolated on those two countries, and for Central Asia, as well.

**The objective of this study** was to assess the incidence rates of prostate cancer depending on ethnicity, age and tumour morphology in Kazakhstan, for the period 2015-2019.

**Materials and methods**

**Ethical Issues**

The study was approved by the ethics committee of Kazakh Medical University of continuing education, Almaty, Kazakhstan (Local Ethics Commission Approval No 21, dated 13.12.2018). In order to form the study cohort, we used patient data on registered cases of prostate cancer incidence in the period 2015-2019.

**Data collection**

The data were obtained from the Electronic Registry of Patients with Oncological Diseases of the Ministry of Health of the Republic of Kazakhstan by forms of medical examinations of patients (www.erob.eicz.kz). In the Electronic Registry of Cancer Patients, the type of cancer, name, date of birth, gender, place of residence, stage and grade of the tumour, as well as information on treatment were systematically recorded. Patients with prostate cancer were included in the database depending on the region of residence. The Prostate Cancer Code (C61) of the 10th revision of the International Classification of Diseases (ICD-10) was used as a method of extraction of the cases of prostate cancer. The data met the USCS publication criteria (http://www.cdc.gov/cancer/npcr/standards.htm) during 2014–2019.

Inclusion criteria: histologically confirmed cases of prostate cancer; diagnosis of primary cancer.

Exclusion criteria: no description of ethnicity; secondary cases identified.

The clinical stage of prostate cancer was determined by the TNM 2002 system, in accordance with the recommendations of the International Union against Cancer and the American Joint Committee on Cancer12. According to age, all patients have been subdivided into 4 categories: <60 yo, 60-69 yo, 70-79 yo and 80+ yo.

According to data from official state statistical sources, more than 130 nationalities reside on the territory of Kazakhstan13. The main ethnic groups are Central Asians (Kazakhs, Uzbeks, Tatars, Kyrgyz, Uighurs, Tajiks, Turkmen, etc.) and Slavonic (Russians, Ukrainians, Belarusians etc.). Other nationalities (Koreans, Germans, Azerbaijanis, Georgians, etc.) make up a small proportion of the population13.

In this regard, in our study, a division into 3 ethnic groups was carried out: Central Asians, Slavs and other nationalities. The incidence rate for other nationalities was not calculated by year due to the diversity of the number of nationalities living in the Republic of Kazakhstan. Nationality was determined by the passport data of patients registered in the state electronic register of oncological diseases.

For the period 2015-2019, in the Republic of Kazakhstan a total of 7354 cases of prostate cancer were registered (Figure 1). Of the total number (n = 7354) of registered cases, 3.69% (n = 272) patients were not included in the study, for the following reasons: 0.7% (n = 51) no description of ethnicity, 0.4% (n = 28) no description of the stage cancer, 2.27% (n = 167) the diagnosis was not established for the first time, 0.35% (n = 26) there was no data on morphological verification of cancer. Thus, the study used data from n = 7082 (96.3%) patients diagnosed with prostate cancer.

**Statistical analysis**

All statistical calculations were performed using SPSS software (version 22.0, IBM SPSS Inc., Chicago, Illinois, USA). A p value < 0.05 was considered statistically significant. Statistical analysis was performed using univariate (no adjustment) and multivariate (with adjustment) analyses. We also received information from the Committee on Statistics of the Ministry of National Economy of the Republic of Kazakhstan on the total population, including the male population by age and nationality. We estimated the incidence of prostate cancer per 10,000 populations based on the male population by age group and nationality. The direct standardization method was used to calculate the age-standardized (ASR) incidence rate14.

**Results**

Among the 7082 patients included in the study, 4363 (61.6%) men were identified as Slavs, 2480 (35.01%) were Central Asians and 239 (3.37%) were identified as other nationalities. The average age
Figure 1. Patient recruitment flowchart.

Figure 2. Standardized incidence rate of prostate cancer in the Kazakhstan regarding ethnicity per 10,000 male population.
in all groups was practically the same, Central Asians 69.22±8.3 years, Slavs 68.66±8.6 years, other nationalities 69.85±8.6 years (p≥0.05) (Table 1).

The results demonstrated that the incidence of prostate cancer prevailed in the age group 60-69 years (p≤0.05) among the Slavs (n = 1870, 42.9%) in comparison with Central Asians (n = 1003, 40.4%), with statistically significant higher rates (p≤0.05). In the age groups <40 and 40-49 years, the lowest incidence of prostate cancer was observed: 0.04% (n = 3) and 0.67% (N = 48) (p ≥ 0.05), respectively, of the total number of diagnosed cases of prostate cancer (n = 7082), but without statistical significance. In the group of Central Asians (n = 268, 10.8%) compared with the Slavs (n = 527, 12.07%), the incidence rates of prostate cancer were lower in patients over the age of 80 years (p≤0.05).

The registered incidence rates of prostate cancer among the Slavs in the first three years of the study were as following: in 2015 – 20.19%, in 2016 – 22.48%
and in 2017 – 22.27%. These figures are higher in comparison with Central Asians, which was regarded as a statistically significant difference (p ≤ 0.05).

In 2019, the number of patients with prostate cancer from the group of other nationalities was 17.57% (n = 42). This number was regarded as the lowest incidence rate in comparison with the Central Asians (p ≤ 0.05).

Regarding the social status, 71.63% (n = 5073) of the total number of registered cases among all ethnic groups were retired persons (p ≤ 0.05).

According to the stages of the tumour process, stage II prevailed (p ≤ 0.05) in the total number of cases (40.32% / n = 2856). The largest number of cases of stage II prostate cancer was identified among the Slavs (n = 1774, 40.66%) in comparison with the Central Asians (n = 987, 39.79%) and other nationalities (n = 95, 39.74%), in whom the incidence rates were considerably lower, with a statistically significant difference (p ≤ 0.05). The next frequently detected was stage III prostate cancer (27.97% / n = 1981), in Central Asians being 26.21% (n = 668), almost two times less in comparison with the Slavs (n = 1240), with a statistically significant difference (p ≤ 0.05). ‘Tumour in situ’ and stage I of malignant neoplasm were less diagnosed tumours types of prostate cancer in the total number of cases, with n = 32 (0.45%) and n = 1119 (15.8%), respectively. The incidence of stage I prostate cancer in the group of Central Asians (n = 368) and in the group of other nationalities (n = 26) was also statistically significant lower in comparison with the incidence among Slavic men (p ≤ 0.05).

By morphological type, adenocarcinoma was the most frequently detected type of prostate cancer (98.4%), and amounted for 97.37% (n = 2415) in Central Asians, 98.85% (n = 4313) in men of Slavic nationality and 99.16% (n = 237) in patients of other ethnic groups. Transitional cell carcinoma and squamous cell carcinoma prevailed in the group of Central Asians, with rates of 1.33% (n = 33) and 0.64% (n = 16), respectively (in comparison with the other two ethnic groups). The sarcomatoid type of tumour was the least detectable form of prostate cancer among all cases (n = 3).

The average incidence in the Republic of Kazakhstan in 2015 was 15.7±1.98 (95% CI (confidence interval): 9.8-17.1). The incidence of prostate cancer in Central Asians in 2015 was less (p≤0.05) 13.3±0.91 (95% CI: 9.8-14.2) than the average for the Slavs 17.1±1.24 (95% CI: 12.4-18.2) per 100,000 male population.

In 2016, the incidence in the Republic of Kazakhstan was 17.6±2 (95% CI: 10.7-18.2). The average annual growth was 1.2%.

The standardized incidence rate was also higher in Slavic nationalities (p≤0.05), 17.8±0.87 (95% CI: 12.3-18.6) than in Central Asians 14.3 ± 0.75 (95% CI: 10.1-16.9), respectively (Table 2, Figure 2).

In 2017, the incidence in the Republic of Kazakhstan was 17.8±1.98 (95% CI: 11.02-18.7). The average annual growth was 2.1%. The incidence rate among Central Asians with prostate cancer in 2017 was also lower (p≤0.05), 14.1±1.01 (95% CI: 10.1-15.1) than among the Slavs 17.6±0.94 (95% CI: 13.3-17.9) per 100,000 male population.

The incidence rate in Kazakhstan for 2018 was 17.1±1.54 (95% CI: 10.9-18.3). The average annual growth was 0.9%. The incidence rate, as in all years, was higher among the Slavs (p≤0.05) 16.4±0.69 (95% CI: 11.7-17.4) than among the Central Asians, 13.7±0.84 (95% CI: 9.7-15.1).

The incidence rate identified in 2019 for the Republic of Kazakhstan was 17.6±1.87 (95% CI: 11.4-18.5). The average annual growth was 1.4%. In comparison with the Central Asians 14.4±0.94 (95% CI: 8.7-17.2), the incidence among the Slavs was also higher (p≤0.05), 16.8±1.1 (95% CI: 8.8-17.7).

The average increase in morbidity for the reference period was the highest in the age group 60-69 years old (1.32 %), and the lowest was detected in the group of 70-79 years old (0.3 %), while the morbidity rate in the group of 50-59 years old was 0.57%.

The correlation analysis showed no significant increase in the incidence of prostate cancer in the age groups: ≤40 yo (r = 0.41, p> 0.05), 40-49 yo (r = 0.31, p> 0.05), +80 yo (r = 0.32, p> 0.05).

**Discussion**

This study is the first on the prevalence of prostate cancer by ethnicity in Kazakhstan and Central Asia. Giving the fact that the ethnic composition of Kazakhstan includes more than 130 different nationalities13, it can be assumed that the data on the prostate cancer for men living in Kazakhstan reflect the incidence rates in Central Asia. The study aimed to assess the incidence rates of prostate cancer depending on ethnicity. It can be useful to understand the dynamics of morbidity in a 5-year time interval and to determine the high-risk groups based on ethnicity and age.

This study and the collected data were fully compliant with the National Cancer Registry Program (NPCR). Overall, 96.3% of prostate cancer cases were included in the study (Figure 1). Duplicate cases were excluded. Only data from the first reported prostate cancer cases were included into the study. Of all reported cases, only 2.27% were excluded from the study due to a secondary diagnosis of prostate...
cancer. The absence of data about patient’s age was not recorded. Information on ethnicity was missing in 0.7% of cases. Prostate cancer stage data were not reported in 0.4% of all cases. In 0.35% of cancer cases, the morphological verification of the tumour was not indicated.

According to the data obtained, the average annual morbidity growth was 2.1%. These rates are low compared to other studies on the incidence of prostate cancer worldwide. According to RCT studies in the United States and Europe, in the period 1989 to 2000, the average annual growth was 8.5%\(^1\). For instance, in Colombia, the annual increase was 3.0% (period 2008-2012)\(^1\).

It has been thought that the early detection of prostate cancer can reduce the mortality rates from this disease, but it can also increase the incidence rates. Apart from that, there is a problem with the over-diagnosis of prostate cancer\(^17\). However, according to one of the latest studies in the United States, it was found that a decrease in the frequency of screening by PSA definition led to an increase in the annual incidence of metastatic prostate cancer\(^15\). Therefore, due to the non-routine nature of screening, it is possible to reduce the rates of possible over-diagnosis and treatment of “indolent” prostate cancer. In addition, it can also lead to the delayed detection of fatal metastatic prostate cancer\(^19\). It should be noted that the screening program by the determination of PSA in the Republic of Kazakhstan was launched in 2012\(^20\). However, during the 5-year period covered by the study (2015-2019), there was no significant increase in the incidence of prostate cancer in Kazakhstan. Perhaps this is attributed to the fact that screening for prostate cancer in Kazakhstan is not a routine procedure. In Kazakhstan, the screening is carried out according to the indications for men in the age categories 50, 54, 58.62 and 66 years with an interval of one time in 4 years\(^20\).

This assumption is the same with the results of the study conducted in Saudi Arabia by Almutairi et al\(^21\). The authors of the study assumed that due to the optional nature of screening, the prevalence of prostate cancer was 2%, which was regarded as low in comparison with other countries. In this regard, to prevent the development of advanced forms of prostate cancer, the reforms in the screening program of this oncological disease are needed. The ethnicity of the patients must be taken into consideration for the screening program.

In our study, the mean age in all groups was practically the same (p \(\geq\) 0.05), in Central Asians 69.22±8.3 years, in Slavs 68.66±8.6 years, and for other nationalities it was 69.85±8.6 years. The mean age of patients with prostate cancer in all ethnic groups was 69.04±8 years, which also corresponds to the age groups described in previous studies\(^22,23\). Our findings indicate the predisposition of old men to the development of prostate cancer, as in previous studies\(^24-27\). In addition, the low incidence rate in men under 40 yo (0.04 %) once again provided the evidence that the prevalence of prostate cancer is closely correlated with the increasing age of the patients\(^28,29\).

As it was described in the previous reports on prostate cancer, morphological verification of the diagnosis was the key factor to confirm the incidence in our study\(^1\). Among all morphological types, the prevalence of adenocarcinoma also confirms the results of published studies in different populations\(^30,31\). In particular, ductal adenocarcinoma has been known for its aggressiveness and a high mortality rate\(^31,32\). According to some reports, the feasibility of developing prostate adenocarcinoma increases from the age of 50 years, and the risk of developing this form of prostate cancer increases in every third person in the age range from 60 to 70 years\(^33\).

Although the average annual increase in the incidence of prostate cancer was not found high, the prevalence of this disease among the Slavs is significantly higher in comparison with the Central Asians. These findings indicate the necessity of highlighting the special role of racial differences in the development of prostate cancer. In general, compared to the
Western population, Asian countries had a lower incidence of prostate cancer.

However, the recent changes in dietary habits and the increase in animal fats and proteins in the diet have led to the growth of the incidence rate of prostate cancer among Asians44. In addition to dietary and environmental factors, the relatively low incidence in Central Asians may be due to the fact that Central Asian men have a higher prevalence of the LL genotype of the polymorphic marker V89L, which has been associated with a lower intraprostatic 5α-reductase activity, and, therefore, a lower risk of developing prostate cancer45.

The preventive strategy against prostate cancer based on the diet regulation has been a matter of debate for many decades36-39. It includes the suggestions that prostate cancer can develop due to the excessive consumption of foods rich in animal fats, however, the use of lycopene, soy products, zinc, selenium and vitamin E for preventive purposes has not found to have a scientific basis yet42. There have also been studies aimed at studying the positive effect of active physical activity on the prevention of prostate cancer41. In addition, it is necessary to also consider that the influence of environmental factors has a significant role in the development of prostate cancer. For example, there are cases when the incidence of prostate cancer among Asians increased because of the migration from countries of origin to the United States. In this regard, it is necessary to recognize that there are no effective preventive measures based on evidence-based medicine42. Therefore, timely diagnostic measures, such as screening in vulnerable groups based on ethnic differences, might help to decrease the morbidity rate. Moreover, according to previous studies among Asians and European men, in addition to determining PSA in the blood, the use of alternative diagnostic methods, such as measuring the Prostate Health Index (PHI) in the blood, with the establishment of different reference ranges of PHI for different ethnic groups, shows optimistic results and is able to determine the high-risk of developing the disease without the risk of over-diagnosis47. A study conducted in a multinational Asian population in Malaysia notes the importance of a different approach in patients from different ethnic groups in diagnostic procedures44.

In conclusion, we found out that the prevalence of prostate cancer among older people in Kazakhstan is quite high. There is a tendency to an increase in the number of patients with this pathology in Kazakhstan in the next future. Such a situation requires further intensive studies and the development of a national strategy for prostate cancer prevention, that should include education of the general population and especially the elderly population (and their families) about prostate cancer. The second important aspect of prevention is regular screening. People diagnosed with prostate cancer should be monitored regularly by multidisciplinary physicians’ teams with a wide range of disease management skills, including counselling for those newly diagnosed.

Study limitations

One of the strengths of our study is that a fairly-long-study period (2015-2019) of the dynamics of the growth of prostate cancer incidence in the research sample of multinational Kazakhstan can be representative of the population of Central Asia. The study also has several limitations. Due to the task of determining the true incidence of prostate cancer by primary diagnosis and avoiding duplication of cases included in the study, the mortality rate of patients was not studied. However, our research may provide a key-step towards understanding optimal strategies for diagnosing prostate cancer in various ethnic groups in Central Asia.

Conclusions

The results of this study showed a relatively low increase in the incidence of prostate cancer in Kazakhstan for the period 2015-2019. However, the relatively high incidence of prostate cancer among men of Slavic nationality than among Central Asians indicates the necessity to optimize the methods of timely diagnosis of prostate cancer, with focus on the ethnic groups at high-risk of incidence.

Author Contributions:

Conceptualization, Z.G. and D.K.; methodology, Zh.I. and N.N.; software, Z.G. and I.F.; validation, A.Zh. and K.N.; formal analysis, Zh.Ch.; investigation, Z.G. and Zh.I.; resources, D.K.; data curation, N.N. and A.Zh.; writing—original draft preparation, K.N., Zh.Ch. and Sh.T.; writing—review and editing, I.R., Z.G., D.K.; visualization, I.R. and N.N.; supervision, Z.G.; project administration, D.K. All the authors have read and agreed with the final version of the article.

Acknowledgments:

The work was carried out within the framework of PhD studies of Z.B. Gassanov in Kazakh Medical University of Continuing Education. All the authors have no conflicts of interest. No financial or nonfinancial benefits have been received or will be received from any party related directly or indirectly to the subject of this article.


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