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Prevalence of Bladder Cancer in the Kerman Province, Southeastern Iran, using the Complete Prevalence Method

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Abstract

Background: Bladder cancer is the 10th most common cancer worldwide. We aimed to assess the prevalence of bladder cancer in the Kerman Province, in southeast Iran.
Materials and Methods: In this cross-sectional study, we used data on 1272 patients with bladder cancer registered in the Kerman population-based cancer registry from 2014 to 2017. There were two parts of data including observed data, including those cases whose information was recorded by the cancer registry, and the unobserved part, including cases before the registry department, was established, to calculate the complete prevalence. The latter was estimated using modeling to be included in the prevalence calculation. The complete prevalence of three-, five-, ten-, and twenty-year of bladder cancer up to the end of 2017 was calculated using rprev package.
Results: A total of 185 (14.54%) women and 1,087 (85.45%) men were recruited. The overall three-, five-, ten-, and twenty-year prevalence of bladder cancer at the end of 2017 was 26.54, 43.46, 80.3, and 142.36 per 100,000 inhabitants, respectively. The prevalence was estimated to be at its lowest rate among both males and females under the age of 45, and at its highest rate among those over 61 and older. In all age groups, males were affected more than females.
Conclusion: The prevalence of bladder cancer in the Kerman Province was higher than the national average and increased with age. Regarding the aging population, policies and programs for prevention, early intervention, and awareness-raising in the community about this cancer are essential.

Keywords: Bladder Neoplasms, Prevalence, Iran.

Introduction

In 2018, bladder cancer was the 10th most common cancer diagnosed worldwide, with approximately 3% of all new cancer diagnoses and 2.1% of all cancer deaths having been related to bladder cancer [1]. In fact, bladder cancer is the

13th most common cause of death among cancers worldwide and the ninth most common cancer in Iran [2, 3]. Iran, with an age-standardized bladder cancer incidence rate of 2.2–3.6 and 7.6-16.1 per 100,000 people in females and males, respectively, in 2018, is one of the relatively high-risk regions in this respect [4]. Worldwide differences in exposure to risk factors, such as smoking, chemical carcinogens in certain occupations, arsenic in drinking water, and endemic chronic urinary infections caused by Schistosoma haematobium are primarily responsible for the differences observed in terms of the occurrence of this cancer. However, a small part of geographical differences could be attributable to differences in accessibility of care and availability of diagnostic procedures [5].

The prevalence index assesses the burden of bladder cancer in a population and determines its spread. In fact, prevalence is itself affected by new cases of a disease and its survival rates [6]. Both direct and indirect methods can be used to estimate the prevalence of cancer. Typically, in direct methods, the information collected is used in population-based surveys, with the validity of which being dependent on the validity of the diagnostic procedures adopted to identify cases of the disease. In most cases, because of the impossibility of performing diagnostic and para-clinical tests in the study population and the asymptomatic nature of the disease in early stages, direct estimation is impossible. In addition, cases identified only from death certificates and problems caused by migration to other healthcare zones after diagnosis can affect estimation validity [7]. In such cases, indirect methods, based on registered health data, can be used as an alternative solution. These methods rely on modeling mathematical relationships among incidence, prevalence, survival, and mortality variables, being used when population-based surveys are not possible due to complexities, costs, and time constraints [8-10]. Population-based cancer registry departments collect information on the incidence of various types of cancer and greatly help assess the status of cancers in a community [11]. The Kerman Population-Based Cancer Registry Program (KPBCR) has been collaborating with a wide range of pathology labs and healthcare providers to collect accurate data on all cancer cases in the community [12]. According to the latest published data, the age-standardized incidence of bladder cancer in the Kerman Province in 2014 was 14.2 per 100,000 inhabitants, which is ranked first among cancers. However, this cancer, with an age-standardized incidence of 8.4 per 100,000 inhabitants, was ranked sixth statewide. In addition, the incidence rate of bladder cancer in men in the Kerman province is six times higher than that in women, being higher than the corresponding national gender-based rate in Iran (3.7) [13, 14].

Health policymakers have been stressing the role of various factors, including high consumption of opium and its derivatives in the province in increasing the rate of this cancer. Additionally, they believe that many other risk factors, including high exposure to fertilizers and chemical pesticides in many parts of the province, existence of mines, and employment of many miners in the region lead to the high incidence of this cancer in the Kerman Province [15-17]. Despite the continuous monitoring of the incidence of this cancer in the province, there is no information available on its prevalence in the community. Policymakers may use the information obtained on the prevalence of bladder cancer to develop health programs, allocate resources, and estimate the burden of the disease. To this end, this study was conducted to determine the prevalence of bladder cancer over three-, five-, ten-, and twenty-year periods up to the end of 2017, using the complete prevalence method in the Kerman Province.

Materials and Methods

In this cross-sectional study, data on 1,272 patients with bladder cancer, who were registered at the Kerman Population-Based Cancer Registry (KPBCR), southeastern Iran, from 2014 to 2017 were utilized. The data included the age, gender, date of bladder cancer diagnosis, life and death status, date of death (in case the person died of bladder cancer), and population of the people at risk in the Kerman province, in 2017. The reason for choosing this time period was incompleteness of the registered data before 2014; thus, only the data registered in 2014 onward were used. Moreover, systematic collection of information on people with cancer in the registration department as well as correcting and cleaning them are time-consuming. In addition, there is usually a 3-4 year gap between diagnosis and registration stages in the registration system, with data on patients being available up to the end of 2017 in the registration department. Thus, patients who lived in the Kerman Province, those who were alive up to the end of 2017, those who were diagnosed with bladder cancer over the past three-, five-, ten- and twenty-years based on medical diagnosis and pathology, and those who were registered in the cancer registration system of the Kerman Province were included in the study. On the other hand,

patients whose time of death and time of registration in the cancer registration system were the same and those whose disease was specified based on their death certificate, were excluded.

The data were received from the cancer registry, and the researcher had no access to patients. In addition, according to the rules of the cancer registry of Iran, all patients' data were used confidentially and anonymously for the purpose of this research. Thus, informed consent forms were not received from the patients.

Measures and statistical analysis: The two forms of partial and complete prevalence could be calculated based on registered health data [6, 18]. Partial prevalence of cancer indicates the ratio of people diagnosed with cancer in a specific time span, who are still alive. In fact, in this type of prevalence, the time span for diagnosing patients must be defined in advance. Since this type of prevalence is calculated based on cancer registry data, the maximum time interval that can be selected is up to the age of the registry department. The main problem, in this respect, is the lack of information in the period before which the cancer registry department was established. Partial prevalence limits the number of patients to those diagnosed within a definite time span [7, 18].

In contrast to partial prevalence, complete prevalence indicates the proportion of the people diagnosed with the disease during a given time period, who survived until the end of the timespan covered by the study. Unlike partial prevalence, complete prevalence is calculated without limiting the diagnosis period [7]. In cases where cancer registry departments were newly established and where there were many unobserved cases whose cancer was diagnosed before the department was established, calculation of this type of prevalence could be accurate and helpful [18].

There existed two types of cases for calculating complete prevalence, which included observed and unobserved cases. Accordingly, the observed cases included those cases whose information was recorded by the cancer registry, yet the unobserved cases included cases existing before the registry department was established. In fact, the latter cases were estimated using modeling as included in prevalence calculation [19]. The following formula is introduced by Capocaccia [7].

Formula 1.

$$N_C(X) = N_U(O, X-L) + N_O(X-L, X) = \int_O^{X-L} I(t)S(t, X-t)\,dt + \int_{X-L}^{X} I(t)S(t, X-t)\,dt$$

NC is the model-based estimate of complete prevalence, which includes a set of unobserved (NU) and observed (NO) estimates as well as a combination of incidence (I) and survival (S) models [7].

The three-, five-, ten-, and twenty-year complete prevalence of bladder cancer, for up to the end of 2017, was calculated using the rprev package in R software 4.0.3. The population at risk in the Kerman Province in 2017, being necessary for estimating the prevalence of bladder cancer, was estimated to be 3,500,000, according to the 2016 census. In fact, the prevalence of three-year, five-year, ten-year, and twenty-year bladder cancer is the ratio of at risk population in the Kerman Province in the given period, who were alive up to the end of 2017 and were diagnosed with bladder cancer over the past three, five, 10, and 20 years, respectively.

Ethical approval was obtained from the Ethics Committee of the Kerman University of Medical Sciences (No. IR.KMU.REC.1398.603).

Results

The present study included 1,272 individuals with bladder cancer, who were registered by the KPBCR from 2014 to 2017 and included 185 women (14.54%) and 1,087 men (85.45%). The mean age of the studied subjects was 62.95 ± 12.61, with 133 (10.44%) persons having been dead at the time of the study. A total of 28 subjects were excluded from the study to avoid inconsistency in statistical analysis, for the time of death and time of registration in the cancer registration system were the same, indicating that their disease was specified based on their death certificate. In addition, among the patients studied, 77 individuals (6.05%) aged under 45, 450 individuals (36.14%) aged 45 to 60, and 717 individuals (57.59%) aged 61 and older. It is worth noting that this classification was done based on a previous study [4], in consultation with experts.

According to the study results, the three-, five-, ten, and twenty-year prevalence of bladder cancer up to the end of 2017, for all ages, and after gender control through the model, was 26.54, 43.46, 80.3, and 142.36 per 100,000, respectively. In fact, these values were calculated separately as well for different age groups, with the age group of 61 and

older having recorded the highest prevalence among all age groups. In addition, the three-, five-, ten-, and twenty-year prevalence of bladder cancer up to the end of 2017, including both genders after age control, was 26.54, 43.46, 80.30, and 142.36 per 100,000, respectively (Table 1).

Table 1. Three-, five-, ten- and twenty-year prevalence of bladder cancer per 100,000 individuals in the Kerman Province at the end of 2017, based on age groups

Prevalence time interval	All ages		Lower than 45 years old		45-60 years old		61 years old and older	
	Number	Prevalence (95% CI)	Number	Prevalence (95% CI)	Number	Prevalence (95% CI)	Number	Prevalence (95% CI)
Three-year	929	26.54 (24.84;28.25)	60	1.71 (1.28; 2.15)	348	9.94 (8.9; 10.99)	521	14.89 (13.61;16.16)
Five-year	1521	43.46 (40.42;46.37)	100	2.86 (2.09; 3.62)	549	15.70 (13.93;17.48)	876	25.02 (22.8;27.24)
Ten-year	2812	80.30 (75.24;84.88)	194	5.55 (4.15; 6.97)	1027	29.35 (26.48;32.27)	1596	45.61 (41.48;49.42)
Twenty-year	4983	142.36 (132.17;153.42)	344	9.83 (5.79;13.97)	1864	53.26 (46.98;59.56)	2801	80.02 (71.89;88.51)

These values were calculated by gender, which show that this cancer was more prevalent in men than in women, with the prevalence in men having been approximately six times higher than that in women for all time intervals (Table 2).

Table 2. Three-, five-, ten-, and twenty-year prevalence of bladder cancer per 100,000 people in the Kerman Province at the end of 2017 by gender

Prevalence time interval	Both genders		Male		Female	
	Number	Prevalence	Number	Prevalence	Number	Prevalence
Three-year	929	26.54 (24.84; 28.25)	794	22.69 (21.11; 24.26)	135	3.86 (3.21; 4.51)
Five-year	1521	43.46 (40.42; 46.37)	1301	37.18 (34.46; 39.86)	220	6.29 (5.18; 7.39)
Ten-year	2812	80.30 (75.24; 84.88)	2405	68.70 (63.99; 73.23)	405	11.57 (9.79; 13.38)
Twenty-year	4983	142.36 (132.17;153.42)	4274	122.11 (111.64;132.42)	729	20.84 (17.26;24.41)

Discussion

Prevalence, commonly reported for the purposes of cancer incidence and survival data, is an essential measure of the burden of a disease in a population, which provides necessary population-based information for researchers and public health officials for future research [20]. According to the present study, the three-, five-, ten-, and twenty-year prevalence of bladder cancer among all age groups after sex control up until 2017 in the Kerman Province was 26.54, 43.46, 80.3, and 142.36 per 100,000 individuals, respectively. In addition, it was found that the prevalence of bladder cancer increased with age, with individuals under age 45 showing the lowest prevalence and those over 61 and older showing the highest prevalence. Additionally, the prevalence of bladder cancer was higher in men than in women, with the ten-year prevalence having been six times higher in men than in women.

These results were in line with a study conducted in Isfahan, one of the central provinces of Iran, which reported that the prevalence of bladder cancer was higher in cases over age 80 and four times higher in men than in women [21]. GLOBOCAN is an online database that provides global cancer statistics and estimates of incidence and mortality rates in 185 countries for 36 types of cancer [22]. According to GLOBOCAN, bladder cancer was the 10th most common cancer worldwide in 2020, with a much higher incidence rate in men; in addition, the age-standardized cancer rate has been four times greater in men than in women. Among different world regions, Asia has the highest five-year prevalence and mortality rate [23]. The five-year prevalence of this cancer in Iran in 2020, for both genders, has been reported to be 17.4 per 100,000 people [23]. However, according to the results of the present study, this ratio in the Kerman Province has been estimated to be 43.5 per 100,000 people, which indicates the very high prevalence of bladder cancer in this province compared to the rest of the country. Accordingly, this can be due to the proximity of this province to the Iranian eastern border with Afghanistan and Pakistan, where the exchange and consumption of narcotics are high in this province, various mines are active in this province, and there is high exposure to agricultural chemical fertilizers. These factors turn careful

follow-ups and policymaking into essential requirements for maintaining human health [24, 25]. A systematic review showed that the highest age-standardized incidence in Iran was observed in the Eastern Azerbaijan Province followed by the Kerman Province [8, 14, 26]. Since prevalence is a function of incidence and survival, the high prevalence observed in our study could have been due to this incidence difference in part. On the other hand, while the integrated national cancer registration system was launched in 2014, and the registered information prior to that year could have been incomplete, the estimated recent increased prevalence might have been due to better case recording as well.

According to the estimates of the World Health Organization (WHO) in 2020, the five-year prevalence of the bladder cancer increased with age [27], being consistent with the results of this study. Research shows that the risk of developing bladder cancer increases with age [28, 29]. Due to the close link between age and the incidence of bladder cancer, one can expect that this disease will pose a serious challenge to the aging population in the coming years. It is worth noting that after measuring the prevalence of the cancer in the Kerman Province by the age group, its five-year prevalence was higher in the age group of less than 45 than that in the whole country. Besides, in the age group of less than 45, the five-year prevalence in the Kerman Province was twice higher than this ratio in the whole country (2.86 per 100,000 people versus 1.2 per 100,000 people, respectively), yet this ratio was not observed in the age groups of 45 to 60 as well as 61 and older [23]. This indicates that the onset age of developing bladder cancer in the Kerman Province is low; although the reason for this is not clear, it is necessary to study the reasons for the low onset age of exposure to risk factors in the Kerman Province compared to the national average.

Consistent with the results of the present study, GLOBOCAN statistics and reports show that the ratio of the five-year prevalence of bladder cancer in Iran is five times higher in men than in women, with the five-year prevalence of 29.4 per 100,000 men and 5.2 per 100,000 women in 2020 [30]. The corresponding ratio in the present study was 37.18 per 100,000 men and 6.29 per 100,000 women, with the former being nearly six times greater than the latter. The reason for such a big ratio is that men are often more likely than women at the risk of cancer due to smoking, drugs, as well as occupational and environmental exposure to carcinogens, such as heavy metals, aromatic amines, organic solvents, and pollutants contributing to bladder cancer. The difference in the prevalence between genders shows the importance of adopting prevention strategies to reduce the prevalence of this cancer, especially in men.

According to the literature review, this study is the first one on determining the prevalence of bladder cancer using the complete prevalence method in the Kerman Province and statewide, which provided valuable information on the status of the cancer in the community. The method of the current study has low costs, needs no demographic surveys, and is routinely based on recorded information; however, some limitations may have affected the study results. Firstly, the accuracy of the recorded information could affect the accuracy of the estimates; secondly, the cancer registry department collected the patients' information from various pathology and clinical references and death certificates, yet some references, such as death certificates may not have had enough credibility. It is hoped that by collecting relevant information from pathology assessments in coming years, we will see an increase in the validity of the recorded data.

Conclusion

The prevalence of bladder cancer in the Kerman Province turned out to be very high compared to the national average, with the incidence of this cancer increasing with age. Iran's age pyramid shows that the population is aging and that people will incur high costs if they get sick. Thus, it is essential to formulate policies and implement programs for the purposes of prevention, early intervention, and raising awareness in the community about this cancer.

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