The epidemiological and histological trend of bladder cancer in Iran

ABSTRACT

Introduction: Bladder cancer is the ninth common cancer in the world, the third common cancer among men in the Arabic and Western Asian countries, and the second in some regions of Iran (a country in the Middle East). There was no study on the epidemiological and histological trend of bladder cancer in Iran. This study aimed to the epidemiological and histological trend of bladder cancer in Iran.

Materials and Methods: In this study, data were extracted from annual cancer registry reports of Iranian Ministry of Health between 2003 and 2008. Standardized incidence rates were calculated using the world standard population and incidence rate was calculated by age groups, sex, and histological type. Data on epidemiologic trend and histology were analyzed using Joinpoint software package.

Results: A total of 23,291 cases were reported. Almost 17.70% (4127 cases) were women and 82.30% (19,170 cases) men. The sex ratio (male to female) was 4.65. Joinpoint analysis showed the significant increased trend of age-standardized incidence rate (ASIR) for both sexes. The annual percentage change of standardized incidence rate was 11.5 (confidence interval [CI]: 9.0–14.0) in women and 10.8 (CI: 8.0–13.6) in men. Two histological types of transitional cell carcinoma (TCC), not otherwise specified and papillary TCC included 43.89% and 49.86% of all cancer cases, respectively.

Conclusion: According to this study the trend of ASIR of bladder cancer in Iran is rising, so it is necessary to conduct further researches in future to provide accurate information on the cancer and investigate related risk factors and implement prevention programs in Iran.

KEY WORDS: Bladder cancer, epidemiology, histological change, Iran, trend

INTRODUCTION

Cancer is one of the major health problems worldwide. It takes account for the third leading cause of death and the second noncommunicable chronic disease. Currently, 12% of deaths occur due to cancer in the world. According to global estimates, there were approximate 12.7 million new cases of cancer and 7.6 million cancer deaths in 2008. It is predicted to increase the incidence of new cases of cancer from 10 million people in 2000 to 15 million people in 2020, which 60% of the changes will occur in developing countries.

The epidemiological pattern of cancer shows the major differences between developed and developing countries. Only 5–10% of cancers are made genetic problems and 90–95% of them environmental factors and individual’s lifestyle. The direct relationship between common cancers, including breast, prostate and colon, and the lifestyle has been observed.

Urinary bladder cancer is one of the most common malignancies in men in the Western countries. One of the important features of the cancer is metastasis to other organs and tissues of the body. This cancer is the ninth common cancer in the world, the third common cancer among men in the Arabic and Western Asian countries, and the second in some regions of Iran (a country in the Middle East). The incidence of cancer has a slow trend in the Western countries. In some areas, it has been stopped, and its mortality rates have remarkably declined. In developing countries, the trend is changing exposure to various risk factors around the world.

In 2008, it was estimated 150,200 new cases of bladder cancer deaths worldwide. Most of these cases were among men, and the mortality rate is different in various countries. The highest incidence rate of cancer has been reported from Europe.
North America, and North Africa. The greatest mortality rate of bladder cancer was reported from Egypt nearly 16.3 cases per 100,000, which was 2 times higher than the highest rate in the European countries.[8] The standardized incidence rate of the cancer in European countries was estimated about 26.9 and 5.3 cases per 100,000 in men and women, respectively.[14]

In the United States, 72,570 new cases of bladder cancer and 15,210 deaths had been reported in 2013.[13]

Smoking and occupational exposure are potential risk factors for cancer in the Western countries and West Asia.[3,11] Chronic infections, such as schistosomiasis, include 50% of cancer cases in some developing countries, especially in Africa.[8]

Histological studies are used as the standard for the diagnosis of bladder cancer and one of the most important prognostic factors in clinical practice.[3,15] The studies revealed that most cancers associated with schistosomiasis are squamous cell carcinoma (SCC), while bladder cancer associated with smoking are transitional cell carcinoma (TCC).[3] Primarily, schistosoma hematobim was considered a potential risk factor in the development of cancer, but currently, the most common type of bladder cancer in Egypt is TCC. Histological studies on clinical samples have shown that lesions were replaced with squamous types, suggested changes in a cause or etiology of bladder cancer over the last 26 years. Polymorphisms available in glutathione-S-transferase genes are also associated with an increased risk of bladder cancer.[16]

Studies in some countries have confirmed changes in the morphology of the cancers.[17,21] It seems to be necessary to investigate the morphology and risk factors of the disease and their changes over time. There was no study on the epidemiological and histological trend of bladder cancer in Iran. This study aimed to the epidemiological and histological trend of bladder cancer in Iran between 2003 and 2008.

MATERIALS AND METHODS

Data source

This is an analytic cross-sectional study, carried out based on reanalysis national registry of cancer (NCR), and disease control and prevention (CDC) report of the Ministry of Health and Medical Education in Iran. Deputy for health of each university is responsible for health issues of the population, and all health activities are managed by these deputies. All deputies for health have been included in the NCR. Registrar would apply the national registration software, which was developed by CDC. Data were collected retrospectively reviewing all new bladder cancer patients in Cancer Registry Center report of health deputy for Iran during a 6 years period (2003–2008).[22] Accordance of the International Classification of Diseases for Oncology (ICD-0: Topography with ICD-OM: Morphology) bladder cancer was defined as ICD-O C42. This study investigated all cases of the morphology of adenocarcinoma, not otherwise specified (NOS) (8140/3), carcinoma, NOS (8010/3), SCC, NOS (8070/3), TCC, NOS (8120/3), and papillary TCC (8130/3).[23]

Statistical analysis

We calculated crude incidence rate and the age-standardized incidence rate (ASIR) per 100,000 persons. We used the direct standardized method using world standard population.[24]

To describe incidence time trends, we carried out joinpoint regression analysis using the software Joinpoint Regression Program, Version 4.1.1.1 (Available from: http://surveillance.cancer.gov/joinpoint/) October 2014. As well to evaluate the morphological changes, we obtained the percentage allocated for kind of morphological types. So to analysis morphology change percentage trends for 6 years, we carried out joinpoint regression analysis using the software Joinpoint Regression Program. The analysis included the logarithmic transformation of the rates, maximum number of one joinpoints, and minimum of 6 years between 0 joinpoints. The test of significance uses a Monte Carlo Permutation method (i.e., it finds “the best fit” line). Joinpoint regression analysis involves fitting a series of joined straight lines on a log scale to the trends. The aim of the approach is to identify possible joinpoints where a significant change in the trend occurs. In this study, 0 joinpoint (full model) was a significant model. The final model selected was the most parsimonious of these, with the estimated annual percentage change (APC) based on the trend within each segment. In describing trends, the terms “significant increase” or “significant decrease” signify that the slope of the trend was statistically significant (P < 0.05). All statistical tests were two-sided.

RESULTS

A total of 23,291 cases were reported. Almost 17.70% (4127 cases) were women and 82.30% (19,170 cases) men. The sex ratio (male to female) was 4.65 [Table 1]. Of the total cases, 21,836 cancer cases were related to two histological types of TCC, NOS and papillary TCC. The number of cases in years studied and in all histological types was more in men than women. Chi-square test showed a significant difference between men and women according to the histology (P = 0.001).

Epidemiologic trend

The standardized incidence rate (per 100,000) increased from 2.12 to 3.78 in women and from 8.35 to 14.42 in men during 2003–2008. Joinpoint analysis showed the significant increased trend of ASIR for both sexes. The APC of standardized method using world standard population.

Table 1: Frequency, crude and standardized incidence of bladder cancer by sex, during the years 2003-2008

| Year | Female | | | Male | | |
|------|--------|---|---|--------|---|---|
| 2003 | 482    | 1.49 | 2.12 | 2263   | 6.63 | 8.35 |
| 2004 | 579    | 1.79 | 2.49 | 2722   | 7.87 | 9.9  |
| 2005 | 689    | 2.01 | 2.86 | 3247   | 8.99 | 11.3 |
| 2006 | 713    | 2.06 | 2.99 | 3364   | 9.3  | 11.66 |
| 2007 | 781    | 2.29 | 3.32 | 3617   | 10.05| 13.03|
| 2008 | 883    | 2.58 | 3.78 | 3957   | 10.99| 14.42|

CIR=Crude incidence rate, ASIR=Age-standardized incidence rate
rate was 11.5 (confidence interval [CI]: 9.0–14.0) in women and 10.8 (CI: 8.0–13.6) in men [Figure 1].

**Morphologic trend**

Two histological types of TCC, NOS and papillary TCC included 43.89% and 49.86% of all cancer cases, respectively. Adenocarcinoma NOS, carcinoma NOS, and SCC NOS included 1.20%, 0.49%, and 1.14% of all cases, respectively [Table 2].

Joinpoint analysis of annual dedicated histology percent showed a significant decline in both sexes for the histology of TCC, NOS. In other histological studied the dedicated percent increased [Table 3].

**DISCUSSION**

The standardized incidence rate of cancer in European countries in 2008 was estimated about 26.9 and 5.3 cases per 100,000 in men and women, respectively.[14] In our study, the rate was 14.42 in men and 3.78 in women in 2008. The rate was lower than findings obtained from European countries but higher than neighboring Arabic countries in both sexes. For example, the standardized incidence rate of the cancer was 10.3 in males and 1.2 in females per 100,000 between 2006 and 2010.[15]

In this study of all cancer, 21,836 cases (93.75%) were TCC, NOS (43.89%) and papillary TCC (49.86%). Adenocarcinoma NOS, carcinoma NOS, and SCC NOS included 1.2%, 0.49%, and 1.14%, respectively. In years studied and in all histological types, the number of cases was more in men than women.

Our findings indicated that 23,291 cancer cases were recorded in Iran during the years of the study. The standardized incidence rate increased from 2.12 to 3.78 in women and from 8.35 to 14.42 in men per 100,000, which was significant for both sexes. APC for ASIR was 11.5 in females and 10.8 in males represented an upward trend between 2003 and 2008. Another study also showed an increasing trend. This was attributed to enhancing life expectancy and increasing the risk of cancer in older ages.[20] In this study, the ratio of males suffering from the cancer was 4.65 times more than women.[20] Some studies reported an increase of risk of bladder cancer in smokers about 2.5 times.[20] Smoking and exposure to toxic substances in the workplace are known as risk factors for cancer.[21,22] A study on the patterns of tobacco use in Iran showed 14.8% of population smoke (26.1% men and 3.2% women).[23] Hence, cancer has been more commonly seen in men.

### Table 2: Distribution of morphology bladder cancer in Iran by sex and year

|       | Female |          |          |          |          |          |          |          |          |
|-------|--------|----------|----------|----------|----------|----------|----------|----------|----------|
|       | n      | %        | n        | %        | n        | %        | n        | %        | n        |
| 2003  | 4      | 0.83     | 14       | 2.42     | 7        | 1.02     | 18       | 2.52     | 16       |
|       |        |          |          |          | 2        | 0.29     | 6        | 0.84     | 8        |
|       |        |          |          |          |          |          |          | 1.02     | 5        |
|       |        |          |          |          |          |          |          | 0.57     |          |
| 2004  | 1      | 0.21     | 2        | 0.35     | 2        | 0.29     | 6        | 0.84     | 8        |
|       |        |          |          |          |          |          |          | 1.02     | 5        |
|       |        |          |          |          |          |          |          | 0.57     |          |
| 2005  | 5      | 1.04     | 6        | 1.04     | 12       | 1.74     | 10       | 1.40     | 11       |
|       |        |          |          |          |          |          |          | 1.41     |          |
|       |        |          |          |          |          |          |          |          | 2.27     |
| 2006  | 310    | 64.32    | 319      | 55.09    | 292      | 42.38    | 285      | 39.97    | 299      |
|       |        |          |          |          |          |          |          | 38.28    |          |
|       |        |          |          |          |          |          |          | 39.38    |          |
|       |        |          |          |          |          |          |          | 33.86    |          |
| 2007  | 157    | 32.57    | 226      | 39.03    | 359      | 52.10    | 340      | 47.69    | 427      |
|       |        |          |          |          |          |          |          | 54.67    |          |
|       |        |          |          |          |          |          |          | 47.7     |          |
| 2008  | 1386   | 61.25    | 1486     | 54.59    | 1319     | 40.62    | 1491     | 44.32    | 1373     |
|       |        |          |          |          |          |          |          | 37.96    |          |
|       |        |          |          |          |          |          |          | 34.47    |          |
|       | 783    | 34.60    | 1133     | 41.62    | 1807     | 55.65    | 1617     | 48.07    | 2018     |
|       |        |          |          |          |          |          |          | 55.79    |          |
|       |        |          |          |          |          |          |          | 57.34    |          |
|       |        |          |          |          |          |          |          |          |          |
| NOS=Not otherwise specified

### Table 3: Joinpoint analyses of cancers percentage allocated to the morphology data for bladder cancer (2003-2008)

|        | Female |          |          |          |          |          |          |          |          |
|--------|--------|----------|----------|----------|----------|----------|----------|----------|----------|
|        | APC    | 95% CI   | APC      | 95% CI   | APC      | 95% CI   | APC      | 95% CI   |
| TCC, NOS | −11.7^  | −15.9−7.3| −10.5^   | −15.3−5.4| −10.7^   | −15.3−5.9|
| SCC, NOS | 10.4^   | 2.6−18.7 | 9.8^     | 1.8−18.4 | 9.9^     | 1.9−18.4 |
| Papillary | 14.0^   | 0.1−29.9 | −1.5     | −9.5−7.3 | 2.5      | −4.0−9.4 |
| Adenocarcinoma, NOS | 16.8 | −12.4−55.7 | 14.2 | −4.6−36.6 | 14.7 | −5.7−39.6 |
| Carcinoma, NOS | 30.3 | −1.6−72.6 | 2.9 | −21.0−34.0 | 6.7 | −16.0−35.6 |

*APC is significantly different from zero at alpha=0.05. CI=Confidence interval, APC=Annual percentage change, NOS=Not otherwise specified.
The annual dedicated histology percent showed a significant decline in both sexes for the histology of TCC, NOS. Recent studies have shown a prevalence of 2–35% for human papillomavirus (HPV) infection in cases of bladder cancer,[26] a study from Iran has demonstrated the presence of HPV in 35.6% of bladder TCC tissue specimens, which was 7 times higher than the control group.[29] It is possible to decrease the incidence of bladder TCC in men and cervical cancer in women through public education regarding the methods of transmission and avoidance of risky sexual behaviors.[28] In other histological studied the dedicated percent increased.

Most cancers associated with schistosomiasis are SCC, while bladder cancer with smoking, is TCC.[31] In a study performed in Egypt, it was found that the number of TCC cases in recent years has increased compared with other morphologies. In other words, TCC cases increased from 22% in 1980 to 73% in 2005, but SCC cases decreased from 78% in 1980 to 27% in 2005. These changes can be due to a reduction in schistosomiasis infection, and an increase of smoking and exposure to chemicals related to the job.[32]

The prevalence of schistosomiasis was 23.8% in centers of the infection in Iran in 1970. The fight against the parasite started in 1958. Preventive measures included diagnosis and treatment of patients, promotion of public health, health education, drying of the marsh and pool, improvement of the environment, digging irrigation channels, and use of molusocide. The measures cause to change the environment and living conditions of parasites and snails and reduce the level of infection about 0.7% in 1979. Continuing the fight and changing the environment lead to eliminate the disease in Khuzestan, South-West of Iran, in 2008. However, there is the disease in the neighboring countries.[33] The upward trend of SCC cases is still observed in patients with bladder cancer between 2003 and 2008. This may be due to lack of data on patients registered in previous years and incomplete entering patient’s information. It is necessary to conduct further researches in future to provide accurate information on cancer.

The limitations of this study were the possibility of incomplete registration or lack of patient’s information, lack of full coverage of the urban and rural population. It seems to carry out proper screening and training for people at risk, the age pattern of cancer should be investigated in the next years. It helps control the disease in the community.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Keyghobadi N, Rafiemanesh H, Mohammadian-Hafshejani A, Enayatrad M, Salehiyini H. Epidemiology and trend of cancers in the province of Kerman: Southeast of Iran. Asian Pac J Cancer Prev 2015;16:1409-13.
2. Ghoncheh M, Mohammadian-Hafshejani A, Salehiyini H. Incidence and mortality of breast cancer and their relationship to development in Asia. Asian Pac J Cancer Prev 2015;16:6081-7.
3. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. CA Cancer J Clin 2011;61:69-90.
4. Vakili M, Pirdehghan A, Adimi M, Sadeghian M, Akhondi M. Epidemiology and trend of cancer in Yazd, a central province of Iran, 2005-2009. J Res Health Sci 2014;14:210-3.
5. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. Int J Cancer 2010;127:2893-917.
6. Chin TM, Tan SH, Lim SE, Iau P, Yong WP, Wong SW, et al. Acceptance, motivators, and barriers in attending breast cancer genetic counseling in Asians. Cancer Detect Prev 2005;29:412-8.
7. Anand P, Kunnumakkara AB, Sundaram C, Harikumar KB, Thrakaran ST, Lai OS, et al. Cancer is a preventable disease that requires major lifestyle changes. Pharm Res 2008;25:2097-116.
8. Weinberg RA, Komaroff AL. Health for life. Your lifestyle, your genes, and cancer. Newsweek 2008;151:40-3.
9. Cegan M, Kolostova K, Matkowski R, Broul M, Schraml J, Fiutowski M, et al. In vitro culturing of viable circulating tumor cells of urinary bladder cancer. Int J Clin Exp Pathol 2014;7:7164-71.
10. Fedewa SA, Soliman AS, Ismail K, Hablas A, Selfield IA, Ramadan M, et al. Incidence analyses of bladder cancer in the Nile delta region of Egypt. Cancer Epidemiol 2009;33:176-81.
11. Roshandel G, Boreini M, Sadjadi A, Malekzadeh R. A diversity of cancer incidence and mortality in west asian populations. Ann Glob Health 2014;80:346-57.
12. Hamdi Cherif M, Serraino D, Mahnane A, Laouamri S, Zaidi Z, Boukharouba H, et al. Time trends of cancer incidence in Setif, Algeria, 1986-2010: An observational study. BMC Cancer 2014;14:637.
13. Parkin DM. The global burden of urinary bladder cancer. Scandinavian journal of urology and nephrology Supplmentum 2008(218):12-20.
14. Ferlay J, Steliarova-Foucher E, Lortet-Tieulent J, Rosso S, Coebergh JW, Comber H, et al. Cancer incidence and mortality patterns in Europe: Estimates for 40 countries in 2012. Eur J Cancer 2013;49:1374-403.
15. Ye F, Wang L, Castillo-Martin M, McBride R, Galsky MD, Zhu J, et al. Biomarkers for bladder cancer management: Present and future. Am J Clin Exp Urol 2014;2:1-14.
16. Salim EI, Moore MA, Bener A, Habib OS, Selif-Eldin IA, Sobue T. Cancer epidemiology in South-West Asia – Past, present and future. Asian Pac J Cancer Prev 2010;11 Suppl 2:33-48.
17. Lönngberg S, Hansen BT, Haldorsen T, Campbell S, Schee K, Ngyard M. Cervical cancer prevented by screening: Long-term incidence trends by morphology in Norway. Int J Cancer 2015;137:1758-64.
18. Almasi Z, Rafiemanesh H, Salehiyini H. Epidemiology characteristics and trends of incidence and mortality of stomach cancer in Iran. Asian Pac J Cancer Prev 2015;16:2757-61.
19. Rafiemanesh H, Rajaei-Bebahani N, Khani Y, Hosseini S, Mohammadian-Hafshejani A, Soltani S, et al. Incidence trend and epidemiology of common cancers in the center of Iran. Glob J Health Sci 2015;8:146.
20. Razi S, Enayatrad M, Mohammadian-Hafshejani A, Salehiyini H, Fahthali-Loy-Dizaji M, Soltani S. The Epidemiology of Skin Cancer and its Trend in Iran. Int J Prev Med 2015;6:64.
21. Razi S, Rafiemanesh H, Ghoncheh M, Khani Y, Salehiyini H. Changing trends of types of skin cancer in Iran. Asian Pac J Cancer Prev 2015;16:4955-8.
22. Goya M. Iranian Annual Cancer Registration Report 2005/2006 Ministry of Health and Medical Education, Health Deputy. Center for Disease Control and Prevention, (Persian). In.; 2007.
23. Fritz AG. International Classification of Diseases for Oncology: ICD-O.
24. Santos SI. Cancer Epidemiology, Principles and Methods. Lyon, France: International Agency for Research on Cancer; 1999.

25. Felix AS, Soliman AS, Khaled H, Zaghoul MS, Banerjee M, El-Baradie M, et al. The changing patterns of bladder cancer in Egypt over the past 26 years. Cancer Causes Control 2008;19:421-9.

26. Zeegers MP, Kellen E, Buntinx F, van den Brandt PA. The association between smoking, beverage consumption, diet and bladder cancer: a systematic literature review. World J Urol 2004;21:392-401.

27. Meysamie A, Ghaletaki R, Haghzali M, Asgari F, Rashidi A, Khalilzadeh O, et al. Pattern of tobacco use among the Iranian adult population: Results of the national Survey of Risk Factors of Non-Communicable Diseases (SuRFNCD-2007). Tob Control 2010;19:125-8.

28. Barghi MR, Rahjoo T, Borghesi M, Hosseini-Moghaddam SM, Amani D, Farrokhi B. Association between the evidence of human papilloma virus infection in bladder transitional cell carcinoma in men and cervical dysplasia in their spouses. Arch Iran Med 2012;15:572-4.

29. Barghi MR, Hajimohammadmehdiarbab A, Moghaddam SM, Kazemi B. Correlation between human papillomavirus infection and bladder transitional cell carcinoma. BMC Infect Dis 2005;5:102.

30. Hamidinia D, Maraghi S, Azimi F, Ai A, Shirian S. The role of climate on prevalence or eradication of vesical schistosomiasis in khuzestan province of Iran. J Parasit Dis 2014:1-3. DOI 10.1007/s12639-014-0515-6.