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.[1,2] 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 approximately 12.7 million new cases of cancer and 7.6 million cancer deaths in 2008.[3] 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.[4,5]

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.[6,7] The direct relationship between common cancers, including breast, prostate and colon, and the lifestyle has been observed.[8]

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.[9] This cancer is the ninth common cancer in the world,[10] the third common cancer among men in the Arabic and Western Asian countries,[11,12] and the second in some regions of Iran (a country in the Middle East).[13] 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.[13]

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.

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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.[10] 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.[16]
In the United States, 72,570 new cases of bladder cancer and
15,210 deaths had been reported in 2013.[15]

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.[12] Histological studies are used as the standard for the diagnosis
of bladder cancer and one of the most important prognostic
factors in clinical practice.[13] 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
hematobiem 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.[14]

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
Classification of Diseases for Oncology (ICD-O: 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
cancer.gov/joinpoint/) October 2014. As well to evaluate the
morphological changes, were 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 incidence
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.

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

<table>
<thead>
<tr>
<th></th>
<th>Female</th>
<th></th>
<th>Male</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>CIR</td>
<td>ASIR</td>
<td>n</td>
</tr>
<tr>
<td>2003</td>
<td>482</td>
<td>1.49</td>
<td>2.12</td>
<td>2263</td>
</tr>
<tr>
<td>2004</td>
<td>579</td>
<td>1.79</td>
<td>2.49</td>
<td>2722</td>
</tr>
<tr>
<td>2005</td>
<td>689</td>
<td>2.01</td>
<td>2.86</td>
<td>3247</td>
</tr>
<tr>
<td>2006</td>
<td>713</td>
<td>2.06</td>
<td>2.99</td>
<td>3364</td>
</tr>
<tr>
<td>2007</td>
<td>781</td>
<td>2.29</td>
<td>3.32</td>
<td>3617</td>
</tr>
<tr>
<td>2008</td>
<td>883</td>
<td>2.58</td>
<td>3.78</td>
<td>3957</td>
</tr>
</tbody>
</table>

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.[13]

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.[10,12,20] 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.[3,13,25] A study on the patterns of tobacco use in Iran showed 14.8% of population smoke (26.1% men and 3.2% women).[27] Hence, cancer has been more commonly seen in men.

The standardized incidence rate of cancer has been more commonly seen in men.

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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.

**Figure 1:** Trends of the standardized incidence rate of bladder cancer by sex in Iran, 2003–2008

<table>
<thead>
<tr>
<th>Year</th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008</td>
<td>19.8</td>
<td>12.0</td>
</tr>
<tr>
<td>2007</td>
<td>16.8</td>
<td>10.4</td>
</tr>
<tr>
<td>2006</td>
<td>13.6</td>
<td>8.7</td>
</tr>
<tr>
<td>2005</td>
<td>10.8</td>
<td>6.1</td>
</tr>
<tr>
<td>2004</td>
<td>8.3</td>
<td>5.7</td>
</tr>
<tr>
<td>2003</td>
<td>6.1</td>
<td>4.2</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Year</th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008</td>
<td>44.0</td>
<td>13.0</td>
</tr>
<tr>
<td>2007</td>
<td>38.0</td>
<td>11.0</td>
</tr>
<tr>
<td>2006</td>
<td>32.0</td>
<td>9.0</td>
</tr>
<tr>
<td>2005</td>
<td>26.0</td>
<td>7.0</td>
</tr>
<tr>
<td>2004</td>
<td>20.0</td>
<td>5.0</td>
</tr>
<tr>
<td>2003</td>
<td>14.0</td>
<td>4.0</td>
</tr>
</tbody>
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<th>Year</th>
<th>Female</th>
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<td>6.1</td>
<td>4.2</td>
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</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Type of Bladder Cancer</th>
<th>Female</th>
<th>Male</th>
<th>Both sex</th>
</tr>
</thead>
<tbody>
<tr>
<td>APC</td>
<td>95% CI</td>
<td>APC</td>
<td>95% CI</td>
</tr>
<tr>
<td>Transitional cell carcinoma, NOS</td>
<td>−11.7^</td>
<td>−15.9–7.3</td>
<td>−10.5^</td>
</tr>
<tr>
<td>Papillary transitional cell carcinoma</td>
<td>10.4^</td>
<td>2.6–18.7</td>
<td>9.8^</td>
</tr>
<tr>
<td>Squamous cell carcinoma, NOS</td>
<td>14.0^</td>
<td>0.1–29.9</td>
<td>−1.5</td>
</tr>
<tr>
<td>Adenocarcinoma, NOS</td>
<td>16.8</td>
<td>−12.4–55.7</td>
<td>14.2</td>
</tr>
<tr>
<td>Carcinoma, NOS</td>
<td>30.3</td>
<td>−1.6–72.6</td>
<td>2.9</td>
</tr>
</tbody>
</table>

^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,[24] 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.[25] 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.[26] In other histological studies the dedicated percent increased.

Most cancers associated with schistosomiasis are SCC, while bladder cancer with smoking, is TCC.[13] 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 by 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.[23]

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 molluscocide. 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.[19] 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.

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Nil.

Conflicts of interest
There are no conflicts of interest.

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