



# TESTICULAR CANCER IN THE WORLD: AN EPIDEMIOLOGICAL REVIEW

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**Abstract – Objective:** Testicular cancer is the most common cancer among male, which occurs between 15-44 years. It is essential to know the incidence, mortality, and risk factors of this disease for proper health planning and effective interventions to reduce its incidence. Therefore, the present study aimed to investigate the incidence and mortality of testicular cancer and its risk factors worldwide.

**Materials and Methods:** The present study reviewed published English studies by searching the databases namely PubMed, Google Scholar and Web of Science until the 2018. The search strategy included the keywords of "Testicular cancer", "Epidemiology", "Incidence", "Mortality", "Risk factors", and "the world". We investigated studies on the incidence, mortality and risk factors of testicular cancer.

**Results:** The incidence of testicular cancer was much lower in Asian, African and Central American countries than European one. The age-standardized incidence rate (ASIR) of testicular cancer was 1.5 per 100,000 people in the world. The highest incidence rate was observed in Europe (7.2-8.7) and the lowest incidence in Africa (0.3-0.6) and Asia (0.4-1.7). The incidence of testicular cancer has increasing trend in Europe and the United States.

**Conclusions:** The highest incidence of this disease was observed in Europe, but the lowest one was in Asia and Africa. Due to the growing incidence of this disease worldwide and the difference in disease trend among populations, further studies on epidemiological characteristics is needed to better understanding of its related risk factors.

**KEYWORDS:** Testicular cancer, Epidemiology, Incidence, Mortality and risk factor.

## INTRODUCTION

Cancer is the most common health problem. It is forecasted that the annual cancer incidence will reach over 20 million worldwide by 2020<sup>1-2</sup>. Testicular cancer is the most common cancer of the gen-

ital system in men<sup>3</sup>. Around 50,000 new cases and 10,000 deaths from testicular cancer are annually diagnosed around the world<sup>4</sup>. The standardized incidence and mortality rate of testicular cancer was equal to 1.5 and 0.3 per 100,000 people in 2012<sup>5</sup>. It is worthwhile to mention here that the incidence



of this disease has risen in European countries and the United States in recent years<sup>6</sup>. The incidence of testicular cancer per 100,000 people was equal to 6.7 among the white men, 1.5 among the American black men, and 4.9 among the Spanish men<sup>7</sup>. However, the incidence of testicular cancer was much lower in Asia<sup>8</sup>, Africa<sup>9</sup> and Central America<sup>10</sup> than European countries. In Asian countries, the highest standardized incidence rates of testicular cancer were reported in Israel (4.9), Georgia (3.3), Turkey (3.2), Lebanon (2.4), and Kazakhstan (2.4 per 100,000 people)<sup>8</sup>. Prevention and early diagnosis of diseases are important factors in controlling and increasing the cancer patients' survival rate<sup>11</sup>. It is significant to note that, despite the elevated incidence of this disease, an appropriate prognosis and a survival rate of 95%, suggest improvement in the survival of this disease in recent decades<sup>13-12</sup>. Two factors, the incidence and mortality, are main epidemiologic factors in assessing the burden of disease among the public<sup>14</sup>. It is essential to know the incidence, mortality and risk factors of this disease for proper health planning and effective interventions to reduce the incidence rate of disease; hence, the present study aimed to investigate the incidence and mortality from the testicular cancer and its risk factors worldwide.

## MATERIALS AND METHODS

The present study reviewed published English studies by 2018 through searching the databases namely PubMed, Google Scholar and Web of Science. The search strategy included the keywords of "Testicular cancer", "Epidemiology", "Incidence", "Mortality", "Risk factors", and "the world". We investigated studies on the incidence, mortality and risk factors of testicular cancer.

## INCIDENCE RATE

In 2015, 8430 new cases of testicular cancer occurred worldwide, and more than 0.5% was observed in the United States. In general, testicular cancer accounts for about 1% of men's cancers around the world<sup>15</sup>. The age standardized incidence rate (ASIR) of this cancer is 1.5 cases per 100,000 people worldwide. This rate is 7.2 in European countries, 6.8 in Australia and New Zealand, from 0.3 to 0.6 in African countries, and 0.4 to 1.7 in Asian countries<sup>16</sup>. It is predicted that the incidence of testicular cancer will increase among all races and ethnic groups from 2013 to 2026. As long as expected incidence of this disease will annually increase by about 3.96% in the United States from 2013 to 2026; hence, the highest

incidence of this disease will occur among Spaniards in the United States<sup>17</sup>.

## MORTALITY

It is estimated that 380 deaths from testicular cancer occurred in 2015<sup>7</sup>. The age-standardized mortality rate (ASMR) of testicular cancer was 0.3 per 100,000 people worldwide and the highest age-standardized mortality rate for this cancer was 0.7 per 100,000 people in Western Asian regions, but the lowest mortality rate was equal to 0.1 in East Asian regions<sup>16</sup>.

## RISK FACTORS OF TESTICULAR CANCER

### GEOGRAPHICAL LOCATION

The incidence of testicular cancer varies and depends on regional differences. It is reported as 0.4 per 100,000 people in Africa, 0.7 in Asia, 5.6 in Europe, 5 in Oceania, and 5 in the United States. In northern Europe, the incidence rate in Denmark and Norway was 2 times higher than that of in Sweden and 4 times higher than that in Finland<sup>18</sup>.

### RACE/ MIGRATION

Despite the fact that testicular cancer models widely vary among countries, the incidence of this disease was higher among whites than other races<sup>19</sup>, so that the incidence of testicular cancer among white Americans was four times higher than blacks ones<sup>18</sup>. An increase in the incidence of this disease in the European race could indicate the industrialization of lifestyles or more exposure to environmental risk factors due to the industrialization. The increasing trend of the incidence of disease in Chile, Argentina, and Brazil in Central and South America could be attributed to the large number of Europeans migrating to these areas. The risk of disease in Swedish men was greater than men who migrated from Finland to Sweden<sup>20</sup>. Furthermore, immigrants from non-European countries to Denmark also demonstrate a lower incidence of disease than the indigenous population of country<sup>21</sup>.

### ECONOMIC- SOCIAL STATUS

The Human Development Index (HDI) is one of the best and most suitable indices of the economic and social status of societies. Several studies<sup>8-22</sup> investigated the relationships between the HDI and the incidence and mortality of testicular cancer; these studies indicated that an increase in the HDI level enhanced the incidence of testicular cancer<sup>5</sup>, consequently, testicular cancer is known as the disease of

rich societies<sup>18</sup>. The incidence of disease was 5.4 in areas with a very high HDI, 2 in areas with a high HDI, 0.5 in areas with a medium HDI, and 0.4 in areas with a low HDI<sup>8-22</sup>.

#### Education

Education is associated with the risk of testicular cancer, so that people with higher education show a higher incidence of disease than others<sup>23</sup>. On the other hand, the low level of education is associated with a delay in diagnosis of this cancer<sup>24</sup>.

#### AGE

The highest number of new cases of testicular cancer occurred in the age group of 15-44 years<sup>25</sup>, so that 15% of cases occurred in 45-year-old men, while only 1% of cases were seen in boys less than 15 years of age<sup>26</sup>. In Africa, 90% of new cases of testicular cancer occurred from 20 to 54 years of age<sup>27</sup>. Also, it is reported that in Ireland, 91% of new cases was seen in the age group of 50 and younger<sup>28</sup>. In 2012, 55266 new cases of testicular cancer were diagnosed worldwide. 52305 (94.64%) were in the age group of 65, and 2961 (36%) in people over the age of 65. Accordingly, new cases of testicular cancer in the world will include 60007, 62903, 65827, and 68351 people in 2020, 2025, 2030 and 2035, respectively. Furthermore, the mortality from this cancer will be 11790, 12781, 13487 and 14886 cases in the mentioned years. The increasing incidence and mortality of this disease is an important point in this regard; hence, there is a need for disease diagnosis at its early stages to improve the quality of life and survival rate of these patients<sup>1</sup>.

#### FAMILY HISTORY

Approximately 2% of new cases of testicular cancer occurred among family members of patients with this cancer<sup>29</sup>, so that the incidence of disease was 8 and 4 times higher in brothers and sons of men with testicular cancer than other people. On the other hand, the age-standardized incidence rate (ASIR) in twin men was 37.5 per 100,000 people<sup>26</sup>.

#### VIRUSES

About 12.1% of diagnosed viruses are associated with a variety of cancers. Besides the highest percentage of cancers by viruses observed in young and middle-aged people. It should be noted that there is a significant association between the exposure to carcinogenic factors and socioeconomic status in individuals and societies. Since, the testicular cancer occurs at the ages of 15 to 40 as well as in the upper economic classes. It is important to mention here that viruses can cause cancer with decades of delay. Accordingly, the odds ratios (OR) for testicular cancer with EBV, CMV, B19 and HIV are equal to 4.8, 1.85, 2.86, and 1.79<sup>30</sup>.

#### OCCUPATION

The incidence of testicular cancer is higher in men who work manually. Metalworkers, farmers, equipment technicians<sup>24</sup>, leather industry workers<sup>26</sup>, and those who are touch with chemical substances such as chemical fertilizers, phenols and foams, are at greater risk for testicular cancer<sup>24</sup>. Firefighters and carpenters, with an incidence of 1.6 and 2.4 per 100,000 people, are the only ones with a significant incidence of testicular cancer<sup>31</sup>.

#### CRYPTORCHIDISM

Cryptorchidism is one of the common diagnostic problems in male infants and is also a major risk factor for testicular cancer and infertility in males later. 2-4% of boys have unilateral or bilateral Cryptorchidism worldwide and 10% of all men with testicular cancer have a history of Cryptorchidism<sup>32</sup>.

#### CHEMICALS

Chemicals like pesticides such as Aldrin, Dieldrin, Enderin, DDT Toxins, Dichlorodiphenyldichloroethylene (DDE) and polycarbonate are associated with the incidence of testicular cancer due to reproductive disorders in men and endocrine disruption<sup>26</sup>.

#### ANTHROPOMETRIC MEASUREMENTS

Several studies have reported a reverse relationship between weight and anthropometric index (body mass index (BMI)). There is a positive relationship between height and testicular cancer. In fact, this disease appears in tall men perhaps due to more calorie intake during the childhood and the influence of puberty hormones on testicular cancer<sup>33,34</sup>.

#### HORMONES

Testicular cancer is related to hormones, so that its incidence is markedly elevated as the puberty begins<sup>35</sup>. According to a meta-analysis study, the precocious puberty does not affect the incidence of testicular cancer, whereas the late puberty can reduce the risk of this disease<sup>36</sup>.

#### MOLECULAR ABNORMALITIES

Generally, 25% of testicular cancer susceptibility is due to genetic factors. The molecular abnormalities associated with testicular cancer include anaplastic, an addition or a loss of some specific chromosomal regions, such as the presence of 12p isochromosome, addition in chromosomes 1, 2p, 7, 8, 12, 14q, 15q, 17q, 21q, X, or deletion in chromosomes 4.5, 11q, 13q, 18q2.(37), Also, 90-95% of testicular tumors are produced by increasing the sex cells that are used to produce tumor gonadostroma<sup>38</sup> and are divided into three categories :(a) prepubertal teratoma-yolk sac tumor, (b) seminoma and nonseminoma, (c) spermatocytic seminoma. Prepubertal tumors are created before puberty, while



seminomas and non-seminomas may expand after puberty, and the third group (spermatocytic seminoma) is created in older men<sup>39</sup>. Immunohistochemistry analysis on seminomas and non-seminomas tumors indicates a decrease in the amount of p53 protein in seminomas and its increase in non-seminomas in most samples. In metastatic testicular cancer, the level of p53 is significantly reduced<sup>40</sup>.

## PHYSICAL ACTIVITY

Childhood physical activity reduces the incidence of testicular cancer in the adulthood. Playing various sports at the ages of 16 to 20 has the preventing effect on the testicular cancer<sup>26</sup>.

## NUTRITION

A high-fat diet is associated with the elevation in incidence of cancer<sup>41</sup>. This association is increased by consumption of dairy products especially milk and cheese<sup>42</sup>. It has been cited that the incidence of testicular cancer has increased due to the high intake of milk and cheese in Scandinavian countries, but the low daily intake of dairy products in Asian and European countries is associated with a reduction in the incidence of testicular cancer<sup>43</sup>.

## SMOKING

Some other studies have reported the association between mothers' smoking and testicular cancer in their offspring<sup>44</sup>. As it is showed in various studies, 16.3% of women smoke during the pregnancy worldwide<sup>45</sup>. There is a strong geographical correlation between smoking in women and the incidence of testicular cancer in Northern Europe countries<sup>44</sup>.

## CONCLUSIONS

The present study aimed to investigate the incidence and mortality of testicular cancer in the world and its relationship between risk factors and the incidence of testicular cancer. The research findings indicated that the age-standardized incidence rate (ASIR) of testicular cancer was equal to 1.5 cases per 100,000 people worldwide and the highest incidence rates were observed in Europe (7.2-8.7), as well as Australia and New Zealand (6.8), and the lowest rates observed in Africa (0.3-0.6) and Asia (0.4-1.7). The most important risk factors for testicular cancer were viruses, hormonal factors, chemicals, age, geographical distribution, race, socioeconomic factors, education, smoking, nutrition, physical activity, occupation, and immigration. Due to the increasing incidence of disease worldwide and the difference in the trend of this disease among populations, there is a need for further studies on patients' epidemiological characteristics in order to better understanding of the risk factors of this disease.

## CONFLICT OF INTEREST:

The Authors declare that they have no conflict of interests

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