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Incidence of cancer in the Turkish Republic of Northern Cyprus

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Background/aim: This study analyzed the incidence, trends, and common types of cancer in the Turkish Republic of Northern Cyprus (TRNC).

Materials and methods: This study is based on data collected from the office of the North Cyprus Cancer Registry, Ministry of Health, for 2007–2012. Data were arranged on the basis of age group, sex, and cancer site. Age standardized incidence rates (ASRs) were estimated with the world standard population. EVIEWS (version 9) software was used for statistical analysis.

Results: Of 1395 registered cases, 52.33% (730) were reported in men and 47.67% (665) in women. The crude incidence rate was 96.41 in men and 101.74 in women. The average annual ASR was 88.88 in men and 87.76 in women with the cumulative rate of 21.47% and 14.69% in men and women, respectively. The most common cancers in men were skin (ASR 15.62), prostate (ASR 11.23), bladder (ASR 11.71), lung (ASR 8.01), and colorectal cancer (ASR 7.61), while in women these were breast (ASR 24.07), thyroid (ASR 14.93), skin (ASR 10.75), colorectal (ASR 6.05), and lymphoma (ASR 4.79). Linear regression analysis confirmed rising trends for both men's (10.79, $P \leq 0.03$) and women's (14.67, $P \leq 0.04$) cancers.

Conclusion: Our findings revealed an increasing trend of cancer incidence in the TRNC. For control and prevention, public awareness of the risk factors and proper screening programs should be recommended.

Key words: Cancer incidence, age standardized rate, cumulative rate, cumulative risk, North Cyprus

1. Introduction

Cancer is a major health issue as a leading cause of death worldwide (1). The global cancer burden is expected to rise by as much as 70% within the next two decades if preventive measures are not implemented (2). Cancers that once were considered the main cause of morbidity and mortality in economically developed countries such as breast, lung, and colon cancer are now frequently diagnosed in developing countries with a higher rate. In recent years alarming trends in cancer incidence rates have been reported in most countries (3,4).

Although the mortality rate has declined, cancer is now the second most important cause of death in Europe; approximately 20%–40% of world cancer deaths are associated with this region. More than three million new cases (54% in men and 46% in women) are registered in Europe each year (5). However, there are great variations in cancer incidences in different European countries, being highest in northern and western parts of Europe while lower in some Mediterranean countries. Prostate cancer is the most common cancer of men in almost all European countries except a few eastern and central countries, whereas lung cancer is still the most common. Among women the breast is the primary site of cancer with the highest incidence rate in western Europe (6,7).

A limited number of studies on cancer incidence have been conducted in the Turkish Republic of Northern Cyprus (TRNC) with a population of approximately 0.3 million (8). However, there is insufficient information on the recent changes in the incidence of common cancer types.

For control and prevention of cancer, both incidence and time-trend analysis are important. Therefore, this study aimed to outline crucial information for policy-makers and decision-makers, stakeholders, cancer researchers, and residents of the TRNC. This study investigated the incidence of cancer and the most commonly occurring types in the TRNC.

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2. Materials and methods

This analytical study was carried out based on data collected from the North Cyprus Cancer Registry (NCCR), TRNC Ministry of Health, for the years 2007, 2008, 2009, 2011, and 2012. The year 2010 is not included in this study since data were not available in the registry. Additionally, no data were recorded after the year 2012 in the registry.

Data sets were arranged on the bases of age groups, sex, and cancer types. Cases with secondary tumors are not included in this study. Only residents of the TRNC with a minimum stay of 6 months before the diagnosis are included in this study.

2.1. Grouping of data

Data analysis was performed separately for men and women in respect to the most common cancer types.

2.2. Parameters studied

2.2.1. Crude rate

Crude incidence rate is used to predict cancer incidence for the current period and is applied to the current population. For each cancer type, crude rate (CR) per 100,000 is calculated by dividing the total cases of respective type by total population: CR = R/N × 100,000, where R = total number of cases and N = total number of person-years (9).

2.2.2. Age standardized rate per 100,000 with world standard population (ASR-W)

Countries with a high proportion of older population have a high percentage of cancer incidence (78% in developed countries) as compared to countries with a high proportion of younger population (58% in developing countries) (10). In such cases, comparisons of crude incidence rates give false outcomes. Therefore, ASR estimation per 100,000 allows for changing population age structure. Standardized incidence rates were calculated by direct standardization method with the world standard population as previously described (11–13). Population values of the TRNC were obtained from census data statistical yearbooks for the years 2007, 2008, 2009, 2011, and 2012 from the State Planning Organization Statistics and Research Department. Variance (Var. ASR) and standard error (S.e. ASR) of age standardized incidence rate were obtained by binomial approximation and 95% confidence intervals (C.I.) were calculated. The formulas used were:

$$\text{ASR} = \frac{\sum_{i=1}^{A} a_i \, \text{w}_i}{\sum_{i=1}^{A} w_i}$$

$$\text{Var (ASR)} = \frac{\sum_{i=1}^{A} (a_i \, \text{w}_i^2 (100\,000 - a_i)/n_i)}{(\sum_{i=1}^{A} w_i)^2}$$

S.e. (ASR) = Var (ASR)

C.I. = ASR ± Za/2 × (S.e. (ASR)) (9).

R = Total number of cases.

N = Total number of person-years.

Σ = Summation, which means the sum of every term in the equation after the summation sign.

a_i = Age specific rate per 100,000 in each age group.

w_i = World standard population in each age group.

n_i = Person-years (every term in the set).

$Z_{a/2}$ = 1.69.

2.2.3. Cumulative rate and cumulative risk

The cumulative rate (the sum over each year of age of the age-specific incidence rate taken from birth to age 74, 0–74 rate) and the cumulative risk (the risk of developing a specific type of cancer at a certain age in the absence of any other cause of death) were calculated with the following formulas:

Cum. rate (0–74) = Σ (age-specific rate × length of age class)

Cum. risk = 100 × (1 –exp (–cum. rate/100)) (14).

The 95% confidence intervals were calculated with the following formula:

C.I. = Cum. rate ASR ± Za/2 × (S.e. (cum. rate)) (9).

2.3. Statistical analysis

Statistical analysis was performed with Excel and EVIEWS (version 9) software. A simple regression model was estimated to calculate the simple linear slope of the annual increase. The significance level was considered as $P \leq 0.05$.

3. Results

In this study, a total of 1395 registered cancer cases have been analyzed between the years 2007 and 2012 (excluding 2010). Of the total registered cases, 730 (52.33%) patients were men and 665 (47.67%) were women. The ASR of cancer showed an increased trend in men as well as in women for the study period of 2007 to 2012. For men, the ASR in 2007 was 71.09 with a rise to 110.12 in 2012. Similarly for women, the ASR in 2007 was 66.04 with an increase to 120.93 in 2012. The highest cancer incidence rate for both sexes was seen in 2011 while the lowest was in 2008 (Table 1).

In men, the most common types of cancer were skin (17% of the total), prostate (12.6%), bladder (12.6%), lung (8.8%), and colorectal (8.63%), while in women they were breast (27.82%), thyroid (16.69%), skin (12.03%), colorectal (7.07%), and lymphoma cancer (5.11%) (Figure 1).

Linear regression analysis indicated a significantly incremental linear slope (10.79) for ASR of cancer for men ($P \leq 0.03$). Linear regression was also significant for ASR of women with an increasing slope of 14.67 ($P \leq 0.04$) (Figures 2 and 3).

The crude incidence rate per 100,000 population was 96.41 in men and 101.74 in women, while the average annual ASR for men was 88.88 ± 6.56 and for women was

Table 1. Year-wise number of cases and age standardized incidence rates (per 10^5) by sex for 2007–2012 (excluding 2010).

Year	Count (men)	Men, ASR/10^5	Count (women)	Women, ASR/10^5
2007	106	71.09	93	66.04
2008	91	59.28	81	57.35
2009	136	83.70	87	59.26
2011	207	116.52	201	125.26
2012	190	110.12	203	120.93

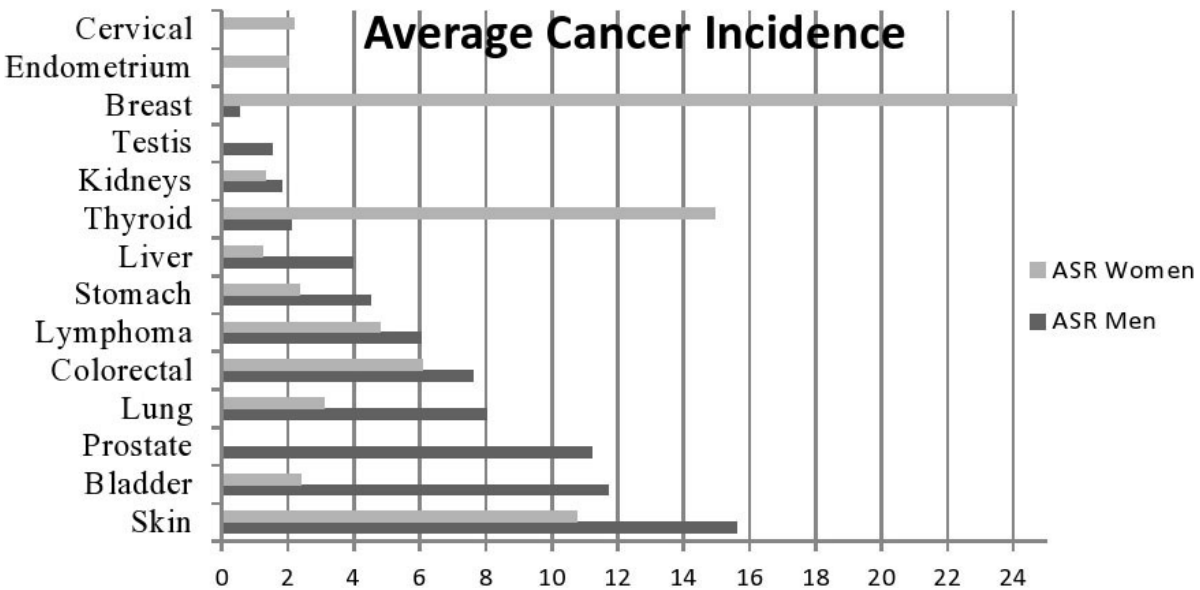

Figure 1. Age standardized incidence rate (per 10^5) for different cancer types by sex in the period 2007–2012 (excluding 2010).

87.71 ± 6.73. The cumulative incidence rate (0–74 years old) was 21.47% in men and 14.69% in women. The risk of developing cancer up to the age of 75 was 19.32% in men and 13.66% in women (Table 2).

Skin cancer (melanoma and nonmelanoma collectively) showed the highest incidence in men with ASR 15.62, cumulative incidence rate of 3.81%, and cumulative risk of 3.74% (Table 2).

The incidence rates of prostate and bladder cancers in men showed some variations with ASR 11.23 and 11.71, respectively. For prostate cancer the cumulative rate was 2.87% and the cumulative risk was 2.82%, while for bladder cancer these were 2.78% and 2.74%, respectively. Lung and colorectal cancers with standardized incidence rates of 8.01 and 7.61 were found to be the fourth and fifth most detected cancer types in men. Apart from the above five, other cancer types in men were lymphoma (ASR 6.05), stomach (ASR 4.52), liver (ASR 3.95), thyroid (ASR 2.11), kidney (ASR 1.82), and testis (ASR 1.53). In men there were also a few registered cases of breast cancer (ASR 0.53) (Table 2).

In women, breast cancer showed the highest incidence with standardized incidence rate of 24.07, followed by thyroid (ASR 14.93), skin (ASR 10.75), colorectal (ASR 6.05), and lymphoma cancer (ASR 4.79). Other forms of cancers identified in women were lung (ASR 3.07), bladder (ASR 2.38), cervix (ASR 2.20), stomach (ASR 2.34), endometrium (ASR 2.01), kidney (ASR 1.30), and liver cancer (ASR 0.60) (Table 2).

Similarly, breast cancer shows the highest cumulative incidence rate and cumulative risk for women in the TRNC (4.0% and 3.92%, respectively) followed by thyroid (2% both) and skin (1.5% both) cancers (Table 2).

4. Discussion

This study investigated the incidence and trend of cancer in the TRNC between the period of 2007 and 2012 (excluding the year 2010). Cancer incidence is on the rise worldwide; hence, an estimated 14.1 million new cancer cases were registered in 2012 while this number was 12.7 million in 2008 (15). In developed countries such as the United States,

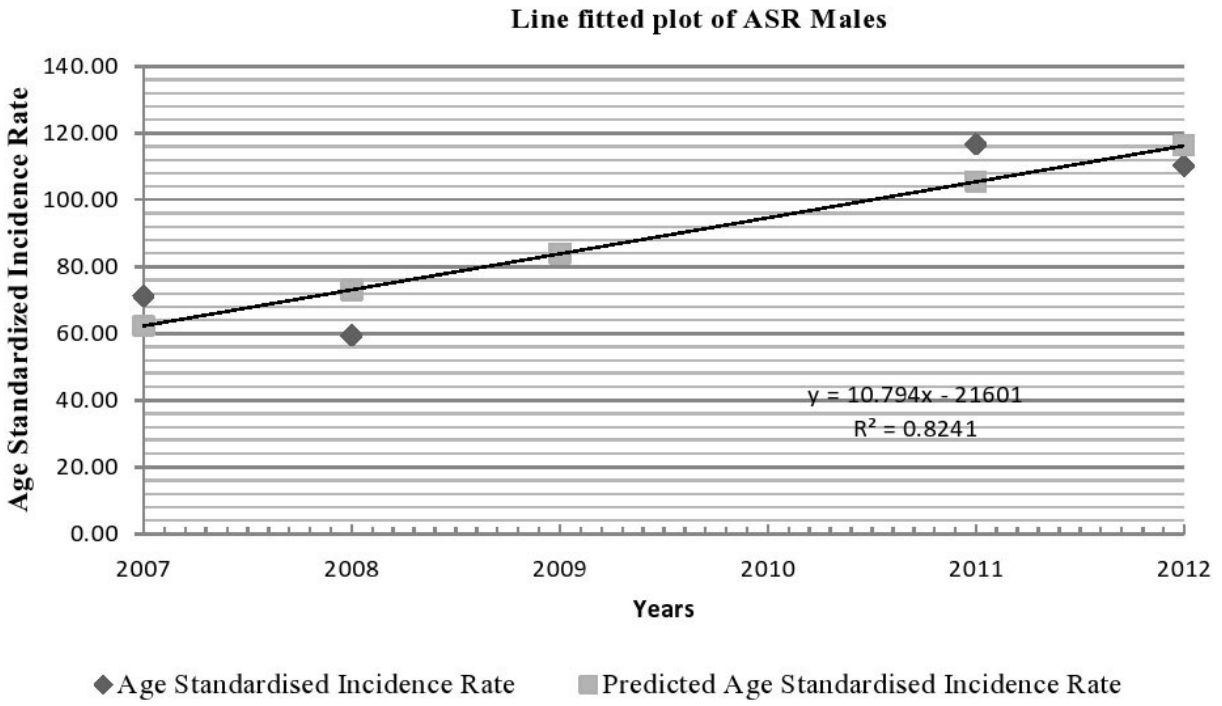

Figure 2. Trend of cancer incidence among men in the TRNC, 2007–2012 (excluding 2010).

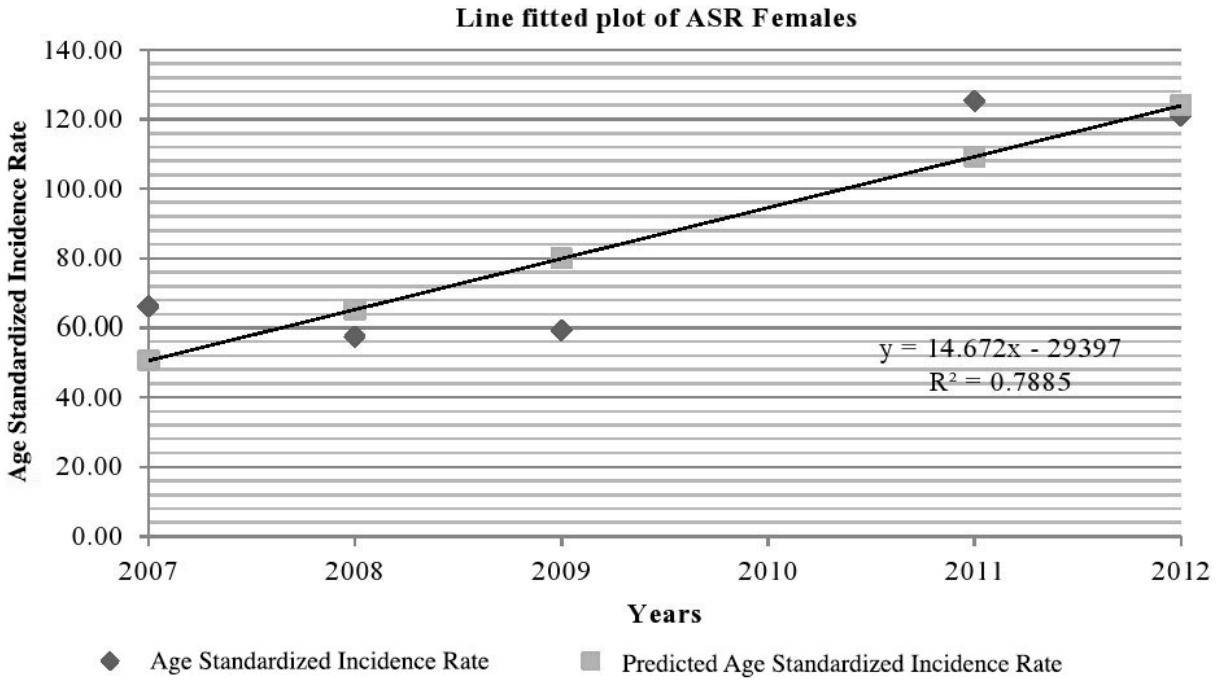

Figure 3. Trend of cancer incidence among women in the TRNC, 2007–2012 (excluding 2010)

more than 50% of men and more than 30% of women have the risk of developing cancer in their lifetime, while in 1950 this risk was 25% for both sexes (16). A similar rise in cancer incidence was observed in many countries such as Belgium, Germany, Mexico, Poland, France, Turkey, the United Kingdom, Norway, Italy, the Netherlands, and Hungary (17). One of the possible reasons for this rise in cancer incidence could be changes in lifestyle (smoking,

Table 2. Crude rate, age standardized rate with world standard population (ASR-W) per 100,000 with 95% confidence interval (C.I.), cumulative rate, and cumulative risk of 12 cancer types by sex, averaged for 5 years (2007–2012, excluding 2010), TRNC.

Cancer type	Crude rate	ASR-W/10^5 with 95% C.I.	% Cumulative rate (0–74) with 95% C.I.	% Cumulative risk (0–74)
Males				
Skin	16.38	15.62 ± 2.78	3.81 ± 0.12	3.74
Bladder	12.15	11.71 ± 2.42	2.78 ± 0.10	2.74
Prostate	12.41	11.23 ± 2.30	2.87 ± 0.11	2.82
Lung	8.45	8.01 ± 1.98	2.86 ± 0.11	2.82
Colorectal	8.32	7.61 ± 1.90	1.39 ± 0.06	1.38
Lymphoma	6.34	6.05 ± 0.44	1.51 ± 0.08	1.49
Stomach	4.75	4.52 ± 1.49	1.49 ± 0.08	1.48
Liver	4.23	3.95 ± 1.39	0.86 ± 0.05	0.86
Thyroid	2.25	2.11 ± 1.01	0.52 ± 0.04	0.52
Kidneys	1.85	1.82 ± 0.96	0.64 ± 0.05	0.63
Testis	1.58	1.53 ± 0.87	0.60 ± 0.05	0.60
Breast	0.53	0.53 ± 0.53	0.07 ± 0.01	0.07
All cancers: males	96.41	88.88 ± 6.56	21.47 ± 0.28	19.32
Females				
Breast	28.30	24.07 ± 3.49	4.00 ± 0.09	3.92
Thyroid	16.98	14.93 ± 1.00	2.00 ± 0.06	1.98
Skin	12.24	10.75 ± 2.38	1.49 ± 0.05	1.47
Colorectal	7.19	6.05 ± 1.75	1.28 ± 0.06	1.27
Lymphoma	5.20	4.79 ± 1.63	0.48 ± 0.02	0.48
Lung	3.52	3.07 ± 1.26	0.45 ± 0.03	0.45
Bladder	2.91	2.38 ± 1.09	0.67 ± 0.04	0.66
Stomach	2.45	2.34 ± 1.10	0.55 ± 0.04	0.55
Cervical	2.60	2.20 ± 0.38	0.53 ± 0.04	0.53
Endometrium	2.75	2.01 ± 1.00	0.52 ± 0.04	0.52
Kidneys	1.53	1.30 ± 0.81	0.25 ± 0.02	0.25
Liver	1.38	1.23 ± 0.81	0.15 ± 0.01	0.15
All cancers: females	101.74	87.71 ± 6.73	14.69 ± 0.17	13.66

obesity, low exercise, etc.) and environmental factors (18,19). Many carcinogens present in our environment in the form of radiation, electromagnetic waves, various types of pathogens, parasites, viruses, chemicals, volatile organic compounds, insecticides and pesticides, food additives, pharmaceutical drugs, compounds in cosmetics, etc. may be among the causes of the current increase in the incidence of cancer worldwide (20).

The world ASR for all cancers excluding nonmelanoma skin cancer is 202.0 in men and 165.2 in women (21). The ASR of all types of cancers for men (88.88) and women (87.71) in the TRNC is as low as half compared to the rest of the world. However, the cancer incidence in the TRNC also shows an increase, which can be clearly noticed by the regression line showing the upward trend for the study period in both sexes. The world cumulative risk of cancer is 20.95% in men and 16.38% in women, while in the TRNC it is 19.32% in men and 13.66% in women. The ASR for other cancer types (colorectal, lung, stomach, liver, and kidney cancers in both sexes and breast and cervical in women and prostate cancer in men) also shows lower incidence in the TRNC than the world for the respective types. However, bladder and thyroid cancers in both sexes showed higher incidence in the TRNC compared to the rest of the world (21) (Table 2).

Hinçal et al. conducted a study on cancer incidence in the TRNC relative to other European countries in the period of 1990–2004. According to their findings, the common cancers in men were lung, skin, colorectal, brain, prostate, bladder, liver, and stomach, while in women they were breast, gynecological, skin, colorectal, lung, liver, brain, stomach, and bladder. Although both studies were based on the same population-based cancer registry (NCCR), the order of prevalence of common cancers differs in our study and this previously published study. This difference might be due to the different time periods of these two studies (1990–2004 versus 2007–2012) and the improvement in the data collection methods by the registry overtime (22). However, it is important to note that both studies showed breast cancer as the most common malignancy of women and skin, bladder, and colorectal cancer were in high prevalence among both sexes in the TRNC (23).

Breast cancer is the most prevalent type in women worldwide with ASR 38.9 and covers about a quarter of all types (21). Breast cancer shows an increasing trend in European countries (24), while in Asian countries the incidence rate of breast cancer is lower but the trend is on rise (25). In the current study the ASR of 24.07 of breast cancer also showed that this cancer is the most common in women in the TRNC with high cum. risk (3.92%), whereas for men, this cancer was shown to be rare with low risk but still existent (0.07%; Table 2). Hormonal therapy, having fewer children, late reproduction, early menarche, late menopause, and obesity are considered to be the risk factors of breast cancer (24,26). Studies also showed the association of prolonged use of oral contraceptives with increased risk of breast cancer (27). For men the risk factors of breast cancer are similar to those for women, including estrogen changes, decreased levels of androgens, benign breast disease, liver and testes disease, Klinefelter syndrome, family history, and exposure to ionization radiations (X-rays, UV rays, etc.), and an obese man has 3–5 times more breast cancer risk than a man of average weight (28).

This study indicated thyroid cancer as the second most prevalent cancer in women in the TRNC after breast cancer with cum. risk of 2.0%. This high incidence of thyroid cancer in women (ASR 14.93) as compared to men (ASR 2.11) requires further investigations to determine whether these findings represent a true increase that could be due to some sort of radiation exposure or are due to frequent use of fine-needle biopsies and ultrasound for small papillary tumor detection (29). A recent report by Farazi also showed a higher rate for thyroid cancer in female Cypriots and reported that the incidence was doubled in just one decade, from 1998 to 2008 (24). Furthermore, the incidence of thyroid cancer has increased in the recent years in other European countries, as well (30). The main risk factors for thyroid cancer are exposure to ionized radiation, mostly in childhood, and a history of thyroid nodules (31).

This study showed a higher incidence rate of skin cancer in both men and women in the TRNC (the 1st most prevalent in men and 3rd in women) with a higher cumulative risk. Skin cancer has been diagnosed with high frequency among men in some parts of the world like New Guinea, Australia, Ireland (32), and Iran (19,33). In 2013 the American Cancer Society reported a link between ultraviolet radiation (UVR) and skin cancer (34). In Cyprus the UVR is considered to be on the high end. Due to the year-round sunshine, the daily ambient UVR level for Cyprus is higher than other countries of the Mediterranean region (35). Other common types of cancer in the TRNC include prostate, bladder, colorectal, lung, liver, kidney, and lymphoma (Hodgkin and non-Hodgkin lymphomas).

Although both lung and bladder cancers are smoking-related, bladder cancer showed a higher ASR as compared to lung cancer in the TRNC. However, as reported previously, genetic and epigenetic alterations in bladder carcinogenesis are linked to environmental and occupational factors and account for a large number of bladder cancer cases in nonsmokers. The interaction between environment and inheritance modulates risk factors for bladder cancer and influences the differing incidences in different populations (36).

Prostate cancer is the third most common cancer among men in TRNC and the second most common in the world, with the highest incidence rate in developed countries (15). The literature is limited about the etiological factors associated with the development and progression of prostate cancer; however, similar to the other cancer types, genetic as well environmental factors contribute to prostate cancer. Older age, family history, and race (African) are the established risk factors (37). Evidence showed that diet and lifestyle mostly affect the risk factors of prostate cancer (38). Other studies found that there is an association between tobacco smoking and the development of many malignancies including larynx, pharynx, esophagus, stomach, pancreas, bladder, uterus, cervix, ovary, and acute myeloid leukemia (39). Tobacco smoking is the main risk factor for triggering cancer and is responsible for 20% of cancer deaths worldwide (2). These tobacco-related cancers show lower incidence rates in Cyprus as compared to other countries of the world (e.g., the United States and United Kingdom) (24). The detailed smoking status of men and women in the TRNC is not known; however, western lifestyle and behavior in addition to genetic predisposition also play a major role in developing such types of cancers (40).

Gynecological cancer (endometrium and cervical) in women showed lower frequency as compared to other types but still has a cumulative risk of 0.52% for

endometrial and 0.53% for cervical cancer in women. The etiology of gynecological cancer is not fully known; however, some studies showed a relation between human papilloma virus infection and cervical cancer (41), while increased numbers of ovarian cycles, abortions, and live births are associated with elevated risks of endometrial cancer (42).

In conclusion, the study findings reveal that cancer incidence showed an increasing trend in the TRNC. Skin cancer in men and breast cancer in women exhibited the highest incidence rates and cumulative risk during this 5-year study. They may be the result of exposure to various risk factors in addition to genetic predisposition. Further studies are required to elucidate the risk factors that are associated with the most prevalent cancers in the TRNC. For cancer control and prevention implementing population-based screening programs, fostering public awareness about the risk factors, and encouraging people for regular screening of the breasts, thyroid, and prostate are recommended.

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