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Epidemiology of Thyroid Cancer in Iran: Incidence, Disability-Adjusted Life Years (DALYs), and Association with Human Development Index (HDI) Using Global Burden of Disease (GBD) Data

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Abstract

Background: Thyroid cancer is the most common malignancy of the endocrine system. Given the differences in its frequency pattern across various parts of the world, understanding the frequency pattern of this cancer in Iran, as well as the burden of this disease, can play a key role in prevention and screening measures. This study aims to examine the incidence of disability-adjusted life years arising from thyroid cancer and the relationship between this disease and the Human Development Index (HDI).

Materials and Methods: This ecological study was undertaken by applying the Global Burden of Disease (GBD) study last version dataset (2021). It explored the pattern of incidence changes from 1990 to 2021 and calculated age—as well as sex-standardized incidence rates per 100,000 populations per year. Regression analysis was utilized to assess time trends and annual mean percentage changes. Finally, incidence rates were estimated separately for each province.

Results: The incidence of thyroid cancer in Iran has grown over the years. This disease's incidence varies across different regions of Iran and directly correlates with the HDI. In some areas, the annual average percentage change (AAPC) has exceeded 20%, indicating serious concern about the rise in this disease.

Conclusion: Overall, the burden of thyroid cancer in Iran has risen from 1990 to 2021, revealing a troubling trend. These changes can assist policymakers and researchers in understanding prevalence patterns as well as health needs more effectively, allowing them to design better programs for controlling and preventing this disease.

Keywords: Thyroid Cancer, Incidence, Disability-Adjusted Life Years, Iran

Introduction

Thyroid cancer is a type of cancer that starts in the thyroid gland, a butterfly-shaped gland located at the front of the neck. Moreover, it is one of the most common malignancies of the endocrine system, accounting for 3% of all cancers [1,2]. In Iran, it ranks as the seventh most common cancer among women and

the eleventh most common cancer among men. Worldwide, there were approximately 233,846 cases of thyroid cancer and 45,575 deaths across all ages in 2019 [3].

There has been a 2.3-fold increase in the incidence of thyroid cancer in many countries across Asia, Europe, South America, and Oceania [4]. In contrast, some countries, such as Norway, Sweden, and Spain, have experienced a decline in the disease [5]. The highest incidence rate of thyroid cancer in the world has been reported in France, with the lowest documented in Pakistan, India, and sub-Saharan Africa [6]. The incidence of thyroid cancer in developed countries is more than twice that of developing countries [7]. The mortality rate of thyroid cancer has been stable and relatively descending. Yet, the recurrence rate of the disease is high, leading to increased complications and the burden of the disease [8].

The thyroid gland plays a critical role in regulating the body's metabolism by secreting thyroid hormones. Thyroid cancer can occur at any age, but it is most common in people aged 25 to 65 [9]. It is more common in women than men, possibly owing to hormonal differences [10]. Other risk factors include environmental and lifestyle factors such as dietary habits, iodine deficiency, exposure to toxic substances, ionizing radiation, the presence of underlying diseases such as metabolic syndrome, insulin resistance, high blood pressure, obesity, gallbladder disease and allergies, a family history of thyroid cancer or thyroid diseases, and Asian ethnicity [11, 12]. Thyroid cancer mortality and Disability-Adjusted Life Years DALYs have also grown by 63.75% and 88.79%, respectively [13]. The main types of thyroid cancer are as follows. Papillary: The most common type that grows slowly. It is often curable and has a good prognosis. Follicular: Includes follicular and Hurthle cell variants and usually responds well to treatment. Medullary: Originates from thyroid C cells and can be hereditary, and its treatment is more complex than the previous two types. Anaplastic: Rare but highly progressive and resistant to treatment. Its prognosis is usually poor [14].

The Human Development Index (HDI) examines a country's economic and social development, capturing three main dimensions: life expectancy, education (measured by the length of schooling and literacy rate), and per capita income. This index is employed to measure quality of life and social well-being. Thyroid cancer is one of the most common types of cancer that has increased in recent years, particularly in societies with high human development indices. The association between HDI and thyroid cancer incidence may indicate the influence of social and economic factors on health and disease prevalence, especially in societies with improved access to health services and diagnostic capabilities [15-17].

It is essential to ascertain the trend of thyroid cancer in various regions before implementing preventive measures. Comparison of the trend and geographic distribution of cancer helps identify areas with a high incidence of the disease explores the relationship between this disease and the Human Development Index (HDI) for thyroid cancer, and provides an opportunity to evaluate the influence of screening programs as well as timely and effective treatment. Thus, this study aimed to analyze the incidence, mortality, disability-adjusted life years, and years of life lost due to mortality from thyroid cancer.

Materials and Methods

The Institute for Health Metrics and Evaluation (IHME) annually updates the Global Burden of Disease (GBD) study, highlighting temporal and geographic trends since 1990. These updates incorporate new data and methodological advancements, providing health policymakers with current information for healthcare planning and resource allocation. The 2019 GBD study estimated the incidence, prevalence, and mortality by age, sex, year, and location for 354 diseases and injuries and 3,484 sequelae (disabling consequences of these diseases and injuries).

This ecological study in Iran was designed to explore the distribution of thyroid cancer incidence, mortality, and disease burden as well as their relationship with the Human Development Index. All data utilized in this study are publicly available at http://ghdx.healthdata.org/gbd-results-tool. The data were extracted using the GBD results tool, which included mortality and incidence estimates for all age and sex groups with 95% confidence intervals. For some indicators, percentage changes between 1990 and 2021 have also been reported.

This study reviews data at both national and subnational levels (by province), allowing for a more detailed analysis of disease incidence and mortality in Iran. The study includes incidence, mortality, and disability-adjusted life years (DALYs). Further, HDI data were extracted and employed from the website (https://globaldatalab.org/shdi) by province.

This study utilized linear regression for analyzing the relationship between the incidence of thyroid cancer and the Human Development Index (HDI). Spatial pattern analysis of thyroid cancer in Iranian provinces was performed using ArcGIS. This study employed the bivariate correlation method to analyze the extracted data as well as explore the correlation between thyroid cancer and the Human Development Index (HDI). The significance level for this analysis was set at $P < 0.05$. Further, the studies were carried out using Stata V-12 (Stata Corp, College Station, TX, USA).

Results

Geographic Fig. 1, Global Incidence of Thyroid Cancer in 2021, based on the Global Burden of Disease (GBD) report, exhibits the uneven distribution of the disease across various regions. Areas such as Eastern Asia and the Middle East, along with parts of the Americas, report a higher incidence of thyroid cancer. This may be linked to genetic, environmental, and lifestyle factors. In contrast, some regions, including Africa and South Asia, indicate a lower incidence rate. This difference may stem from inadequate diagnosis, poor case recording, or environmental variations.

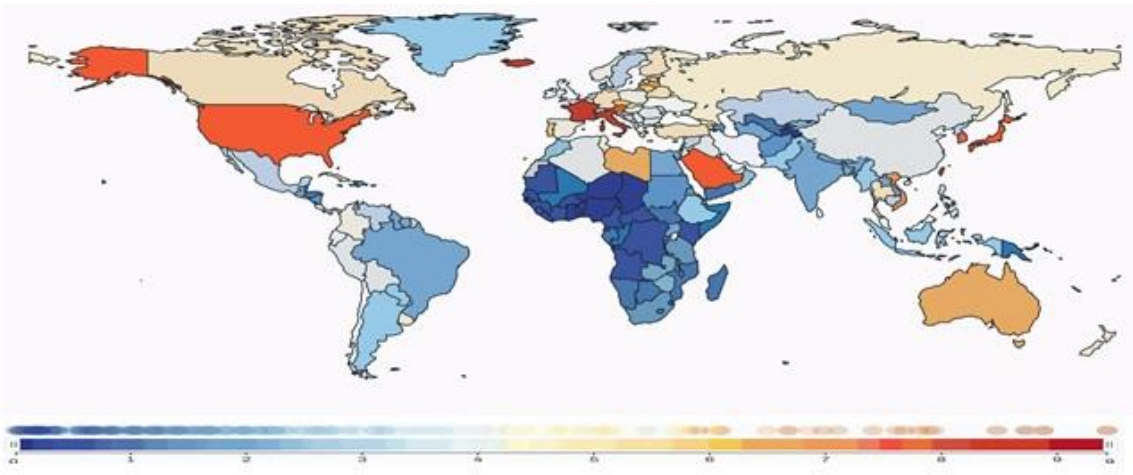


Fig. 1. Age-standardized incidence of thyroid cancer in both sexes worldwide in 2021

Table 1 reports the forecast of the number of new cases of thyroid cancer from 2022 to 2045 in different regions of the world. Based on the data, the number of new cases is expected to grow the most in Africa, with an increase of 102.7%. In Asia, a growth of 23.7% is also possible, indicating a significant rise in the disease burden on this continent. In Europe, a reduction of 3.8% is observed, which may reflect improvements in diagnosis and treatment. Also, in North America and Oceania, increases of 39.8% and 52.7% are expected, respectively. These changes reflect the need for greater attention to thyroid cancer and appropriate health planning in regions with an increase in new cases.

Table 1. Estimated number of new cases of thyroid cancer from 2022 to 2045, incidence, both sexes, age 0- 85+

Population	Annual population		Number of new cancer cases		Change in number
	2022	2045	2022	2045	
Africa	1406728760	2 289 760 665	19 740	40 006	**+102.7%**
Asia	4648273841	5248927585	596599	737766	**+23.7%**
Europa	747 543 827	713 604 953	78 552	75 541	**-3.8%**
Latin America and the Caribbean	665450799	742 562 073	63 530	84 574	**+33.1%**
Northern America	373 318 358	416 765 998	57 747	66 207	**+14.7%**
Oceania	43755196	55922350	5046	7052	**+39.8%**

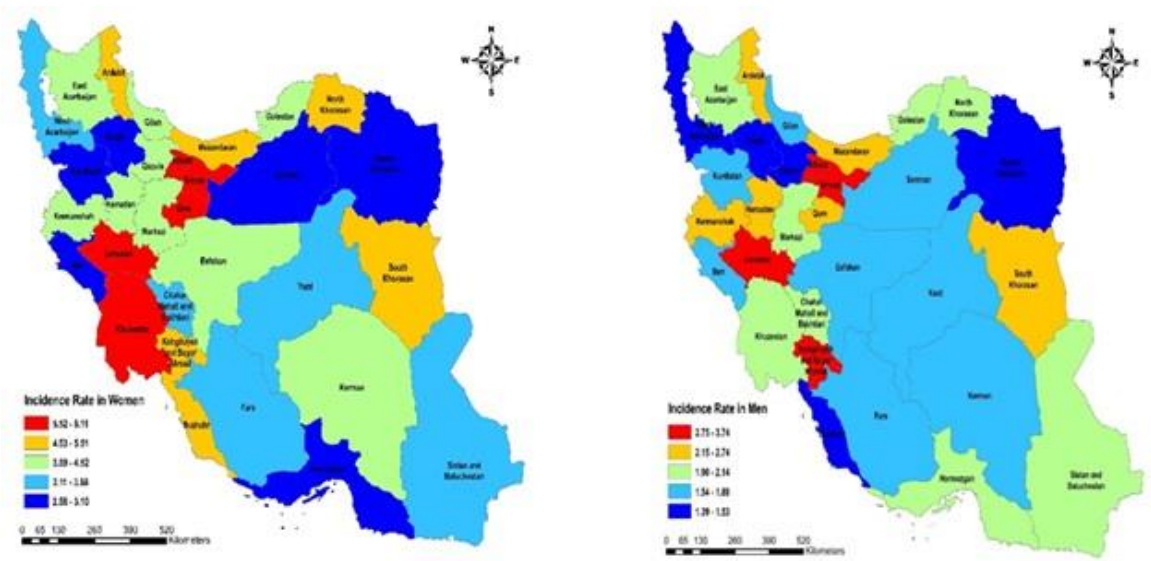


Fig. 2. The incidence rate of thyroid cancer in Iranian men and women in 2021

The ascending trend of thyroid cancer incidence in Iran from 1990 to 2021 indicates a concerning pattern, particularly evident in recent years. Since 1990, the incidence of thyroid cancer in Iran has grown steadily, with this increase being especially noticeable in recent decades. According to some reports, the incidence rate for this type of cancer in the 1990s was fewer than 2 cases per 100,000 people and has gradually escalated to more than 7 cases per 100,000 people in recent years. According to the Global Burden of Disease (GBD) report, this increment in incidence is most pronounced in the age group of 50 to 75 years, with the occurrence in women reported to be about three times higher than that in men (Fig. 2, 3).

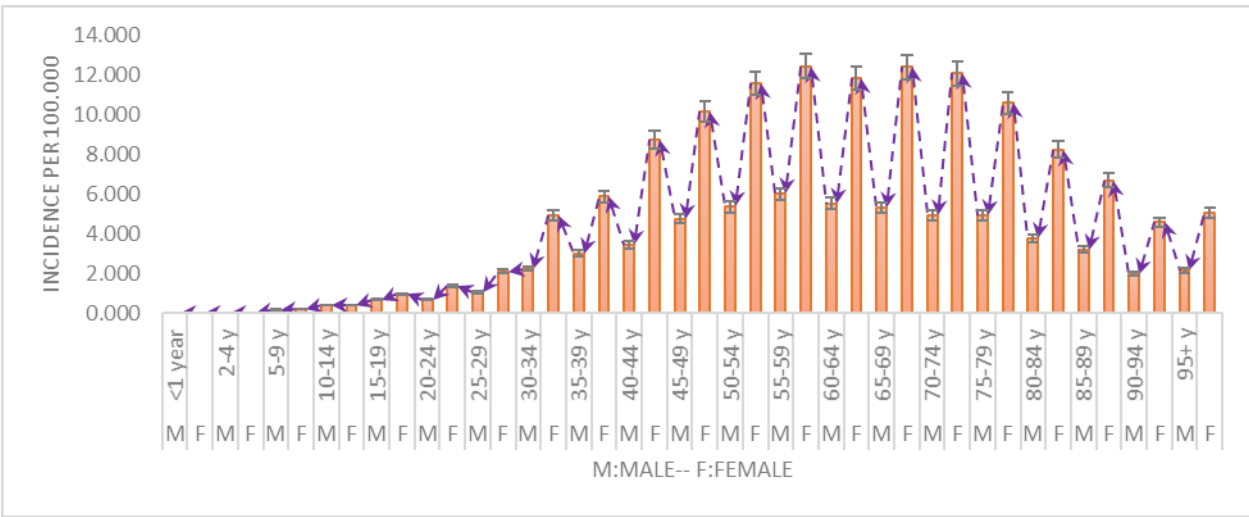


Fig. 3. The incidence rate of thyroid cancer by other age groups in both sexes in Iran – 2021

Table 2 presents data on the incidence of thyroid cancer across the Iranian population from 1990 to 2021. This data is categorized by gender (men and women) and various regions of Iran (Fig.4). Overall, the incidence of thyroid cancer in Iran has risen over the years. This increment may be attributed to several factors, including lifestyle changes, heightened awareness, and early disease diagnosis. In many regions, the incidence of thyroid cancer in women is significantly higher than in men. Also, according to findings from other studies, this disparity in incidence between the two sexes has reached three times greater in some areas, potentially linked to hormonal and genetic factors that impact women more. The incidence of this disease varies across different areas of Iran. For instance, in regions such as Bushehr, Ilam, Kermanshah, Zanjan, Semnan, and North Khorasan, it is somehow low in both sexes. In contrast, in other areas such as Tehran, Qazvin, Markazi, and Khuzestan, the incidence is considerably higher in women. Nevertheless, the incidence is far greater in men in Kohgiluyeh and Boyer-Ahmad, Lorestan, Tehran, and Qazvin. These variations can be associated with environmental, genetic, and social factors. The Average Annual Percent Change (AAPC) in specific regions reveals a significant rise in the incidence of thyroid cancer. For example, in some areas, the AAPC has exceeded 20%, raising serious concerns about the growing prevalence of this disease.

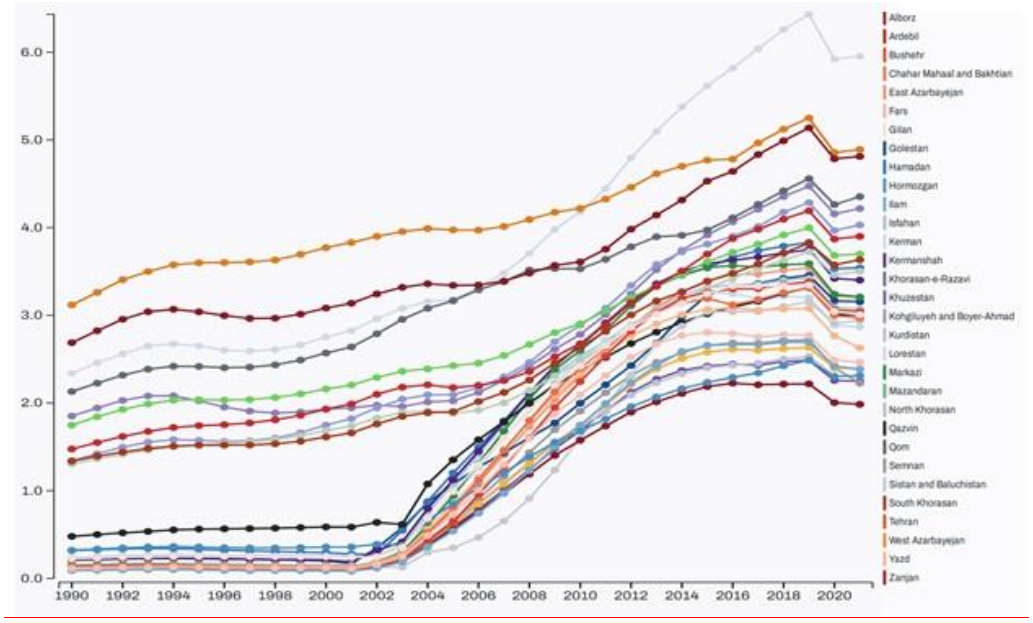


Fig. 4. Age-standardized incidence of thyroid cancer in Iranian men and women from 1990 to 2021

Table 2. The incidence of thyroid cancer across the Iranian population from 1990 to 2021

Region	1990		2000		2010		2021		Average Annual Percent Change (AAPC) 1990-2021
	Male	Female	Male	Female	Male	Female	Male	Female	Both Sex
Alborz	3.7 (3.1-4.9)	4.37 (1.43-6.67)	1.44 (0.60-2.03)	4.97 (1.98-7.30)	2.10 (0.79-2.87)	5.28 (1.95-7.26)	3.33 (1.03-4.90)	6.38 (1.94-9.67)	0.79 (0.23-1.62)
Ardebil	0.64 (0.36-0.90)	2.37 (1.13-6.63)	0.84 (0.46-1.17)	3.03 (1.55-4.12)	1.52 (0.69-2.00)	3.82 (1.45-5.28)	2.30 (0.90-3.15)	5.51 (1.93-7.88)	1.64 (0.60-2.98)
Bushehr	0.04 (0.01-0.24)	0.17 (0.03-0.95)	0.04 (0.00-0.24)	0.17 (0.02-0.99)	0.93 (0.56-1.15)	3.76 (1.67-5.12)	1.41 (0.85-1.96)	4.80 (1.83-7.20)	28.14 (2.31-225.46)
Chahar Mahaal and Bakhtiari	0.07 (0.02-0.38)	0.21 (0.04-1.13)	0.06 (0.01-0.37)	0.19 (0.03-1.16)	1.50 (0.59-2.04)	3.29 (1.47-4.57)	2.07 (0.79-3.09)	3.88 (1.69-5.71)	20.74 (1.62-123.13)
East Azarbayejan	0.06 (0.01-0.35)	0.20 (0.04-1.09)	0.06 (0.01-0.36)	0.20 (0.03-1.09)	1.37 (0.62-1.82)	3.25 (1.66-4.47)	2.11 (0.85-3.06)	4.32 (1.89-6.49)	23.79 (1.86-138.05)
Fars	0.05 (0.01-0.33)	0.17 (0.02-0.99)	0.06 (0.01-0.39)	0.18 (0.02-1.06)	1.22 (0.80-1.62)	2.97 (1.94-3.92)	1.63 (0.98-2.32)	3.32 (2.08-4.73)	20.98 (2.22-160.97)
Gilan	0.10 (0.03-0.46)	0.35 (0.10-1.56)	0.12 (0.04-0.56)	0.37 (0.10-1.81)	1.39 (0.82-1.79)	3.42 (2.02-4.49)	1.89 (1.02-2.63)	4.11 (2.09-6.23)	12.34 (1.17-50.33)
Golestan	0.11 (0.04-0.46)	0.33 (0.10-1.38)	0.10 (0.03-0.46)	0.30 (0.07-1.48)	1.37 (0.66-1.80)	2.60 (1.66-3.35)	2.14 (0.79-3.13)	4.13 (2.10-5.74)	13.50 (1.21-46.66)
Hamadan	0.18 (0.09-0.48)	0.46 (0.20-1.51)	0.16 (0.08-0.56)	0.42 (0.17-1.71)	1.86 (0.71-2.52)	3.44 (1.69-4.47)	2.74 (0.81-4.15)	4.35 (1.72-6.32)	10.14 (0.75-25.41)
Hormozgan	0.21 (0.13-0.46)	0.44 (0.19-1.44)	0.22 (0.14-0.56)	0.50 (0.24-1.69)	1.30 (0.59-1.73)	2.06 (1.39-2.65)	2.02 (0.79-2.95)	2.62 (1.55-3.64)	6.21 (0.77-14.52)
Ilam	0.05 (0.01-0.30)	0.14 (0.01-0.77)	0.05 (0.01-0.31)	0.13 (0.01-0.77)	1.22 (0.78-1.57)	2.26 (1.73-3.05)	1.71 (0.97-2.34)	3.04 (2.08-4.18)	25.46 (3.09-214-30)
Isfahan	0.10 (0.03-0.47)	0.37 (0.12-1.58)	0.12 (0.04- 0.57)	0.40 (0.13-1.80)	1.38 (0.75-1.78)	3.73 (1.60-5.12)	1.83 (0.95-2.50)	4.35 (1.72-6.32)	12.17 (1.06-43.95)
Kerman	0.07 (0.02-0.38)	0.20 (0.04-1.06)	0.07 (0.02-0.42)	0.22 (0.04-1.19)	1.46 (0.68-1.98)	3.50 (1.58-4.84)	1.78 (0.82-2.61)	4.01 (1.74-5.86)	20.59 (1.48-123.02)
Kermanshah	0.11 (0.04-0.46)	0.32 (0.08-1.37)	0.08 (0.02-0.41)	0.23 (0.05-1.19)	1.70 (0.68-2.27)	3.62 (1.86-4.85)	2.35 (80-3.44)	4.43 (1.97-6.62)	15.31 (1.13-57.73)
Khorasan-e-Razavi	0.05 (0.01-0.27)	0.15 (0.02-0.85)	0.05 (0.01-0.30)	0.16 (0.02-0.91)	0.99 (0.62-1.29)	2.36 (1.53-3.13)	1.39 (0.78-1.97)	3.10 (1.80-4.32)	21.96 (2.17-163.86)
Khuzestan	0.65 (0.40-0.90)	3.12 (1.32-4.97)	0.69 (0.52-0.87)	3.26 (1.74-4.48)	1.27 (0.67-1.60)	4.31 (1.61-5.77)	1.98 (0.89-2.79)	6.49 (1.98-9.83)	1.28 (0.37-2.47)
Kohgiluyeh and Boyer-Ahmad	0.83 (0.36-1.22)	1.93 (1.15-2.51)	1.09 (0.47-1.51)	2.46 (1.56-3.30)	2.00 (0.67-2.75)	3.78 (1.89-5.22)	3.06 (0.93-4.56)	5.04 (2.31-7.30)	2.00 (0.80-3.34)
Kurdistan	0.08 (0.03-0.38)	0.23 (0.06-1.12)	0.08 (0.02-0.41)	0.23 (0.05-1.19)	1.15 (0.66-1.51)	2.32 (1.43-3.03)	1.68 (0.79-2.46)	2.94 (1.63-4.14)	13.87 (1.29-56.70)
Lorestan	1.11 (0.36-1.73)	3.70 (1.06-6.02)	1.34 (0.51-1.89)	4.25 (1.49-6.01)	2.42 (0.72-3.36)	5.89 (1.50-8.34)	3.74 (0.91-5.58)	8.11 (1.8312.38)	1.55 (0.52-2.62)
Markazi	0.07 (0.02-0.38)	0.22 (0.05-1.13)	0.07 (0.01-0.41)	0.22 (0.04-1.16)	1.58 (0.71-2.09)	3.62 (1.52-5.12)	2.12 (0.90-3.11)	4.30 (1.68-6.37)	20.71 (1.27-114.96)
Mazandaran	0.89 (0.46-1.73)	2.61 (1.39-3.90)	1.16 (0.59-1.62)	3.16 (1.90-4.26)	1.85 (0.86-2.54)	3.95 (1.97-5.07)	2.53 (0.97-3.65)	4.86 (2.18-7.22)	1.12 (0.43-2.08)

North Khorasan	0.67 (0.32-0.96)	1.97 (1.05-2.90)	0.88 (1.18-0.44)	2.50 (1.42-3.29)	1.49 (0.60-2.00)	3.43 (1.49-5.52)	2.11 (0.75-3.08)	4.87 (1.85-7.06)	1.69 (0.65-3.00)
Qazvin	0. 16 (0.08-0.46)	0.81 (0.45-1.76)	0.20 (0.10-0.60)	0.99 (0.62-2.30)	1.06 (0.69-1.31)	3.68 (1.48-5.01)	1.53 (0.94-2.09)	4.52 (1.64-6.78)	5.27 (0.57-12.38)
Qom	0.93 (0.40-1.41)	3.43 (1.12-5.43)	1.18 (0.55-1.61)	4.10 (1.45-5.62)	1.73 (0.69-2.29)	5.43 (1.55-7.56)	2.52 (0.88-3.70)	6.28 (1.56-9.39)	1.04 (0.35-1.98)
Semnan	0.07 (0.01-0.34)	0.16 (0.02-0.90)	0.07 (0.01-0.40)	0.16 (0.02-0.94)	1.44 (0.70-1.92)	2.38 (1.58-3.06)	1.83 (0.79-2.67)	2.63 (1.52-3.73)	18.84 (1.68-130.09)
Sistan and Baluchistan	0.05 (0.01-0.28)	0.13 (0.02-0.70)	0.06 (0.02-0.33)	0.17 (0.03-0.90)	1.07 (0.42-1.46)	2.12 (1.21-2.94)	2.00 (0.53-3.00)	3.88 (1.52-5.70)	31.60 (2.17-176.28)
South Khorasan	0.73 (0.29-1.06)	1.98 (0.78-3.04)	0.91 (0.37-1.27)	2.32 (1.03-3.16)	1.62 (0.52-2.19)	3.62 (1.31-4.95)	2.38 (0.64-3.55)	4.84 (1.39-7.28)	1.72 (0.62-2.93)
Tehran	1.50 (0.44-2.19)	4.87 (1.26-9.94)	1.91 (0.64-2.66)	5.80 (1.77-8.50)	2.45 (0.72-3.37)	6.05 (1.77-8.74)	3.17 (0.92-4.69)	6.63 (1.73-10.21)	0.57 (0.10-1.27)
West Azarbayejan	0.05 (0.01-0.30)	0.16 (0.02-0.87)	0.05 (0.01-0.30)	0.16 (0.02-0.91)	1.00 (0.62-1.52)	2.49 (1.51-3.28)	1.41 (0.75-1.94)	3.37 (1.91-4.80)	22.00 (2.25-160.04)
Yazd	0.06 (0.01-0.33)	0.22 (0.04-1.11)	0.06 (0.01-0.37)	0.22 (0.03-1.27)	1.21 (0.75-1.54)	3.51 (1.64-4.89)	1.63 (0.86-2.38)	3.70 (1.56-5.38)	18.20 (1.45-112.43)
Zanjan	0.05 (0.01-0.29)	0.13 (0.02-0.79)	0.05 (0.01-0.30)	0.14 (0.01-0.83)	1.03 (0.68-1.31)	2.10 (1.35-2.81)	1.41 (0.81-1.96)	2.56 (1.46-3.61)	20.82 (2.34-154.95)

Table 3. DALYs (YLDs and YLLs) of thyroid cancer and Average Annual Percent Change (AAPC) 1990-2021 across the Iranian population from 1990 to 2021

Region	**1990 Both sex**			**2015 Both sex**			**2021 Both sex**			**Average Annual Percent Change (AAPC) 1990-2021**		
	DALYs	**YLDs**	**YLLs**	**DALYs**	**YLDs**	**YLLs**	**DALYs**	**YLDs**	**YLLs**	**DALYs**	**YLDs**	**YLLs**
Alborz	11.54 (4.42-5.95)	1.33 (0.44-2.23)	10.20 (3.96-14.01)	12.62 (4.24-16.62)	2.29 (0.68-3.65)	10.33 (3.55-13.46)	12.14 (4.01-16.94)	2.44 (0.72-4.03)	9.69 (3.27-13.38)	0.05 (-0.22-0.50)	0.82 (0.21-1.77)	-0.04 (-0.29-0.34)
Ardebil	7.70 (4.39-10.43)	0.73 (0.36-1.20)	6.96 (3.95-9.46)	11.40 (4.42-14.42)	1.87 (0.63-3.01)	9.52 (3.69-11.88)	10.79 (4.18-14.17)	1.97 (0.68-3.06)	8.81 (3.50-11.45)	0.40 (-0.13-0.99)	1.69 (0.49-3.29)	0.26 (-0.21-0.80)
Bushehr	0.49 (0.07-2.56)	0.05 (0.00-0.30)	0.44 (0.06-2.28)	9.67 (4.24-12.77)	1.64 (0.59-2.66)	8.03 (3.56-10.25)	7.88 (3.87-10.72)	1.53 (0.63-2.53)	6.35 (3.24-8.52)	14.93 (0.90-121)	27.31 (2.12-219.23)	13.41 (0.76-109.05)
Chahar Mahaal and Bakhtiari	0.61 (0.13-2.98)	0.07 (0.01-0.37)	0.54 (0.12-2.62)	8.71 (3.32-11.60)	1.62 (0.57-2.58)	7.08 (2.68-9.22)	6.83 (3.14-9.20)	1.51 (0.65-2.44)	5.32 (2.47-7.07)	10.04 (0.36-58.65)	20.23 (1.46-119.80)	8.72 (0.42-62.44)
East Azarbayejan	0.71 (0.15-3.61)	0.06 (0.01-0.36)	0.64 (0.14-3.26)	11.46 (4.58-15.02)	1.71 (0.57-2.58)	9.75 (3.88-12.55)	9.40 (4.38-12.48)	1.62 (0.67-2.65)	7.77 (3.64-10.24)	12.22 (0.59-69.89)	23.46 (1.78-137.98)	11.06 (0.42-62.44)
Fars	0.52 (0.08-2.81)	0.05 (0.00-0.32)	0.46 (0.07-2.50)	8.16 (4.73-10.41)	1.42 (0.72-2.23)	6.74 (3.97-8.53)	6.45 (4.36-8.29)	1.24 (0.73-1.87)	5.21 (3.48-6.65)	11.22 (0.91-86.03)	20.31 (2.11-158.44)	10.09 (0.72-78.25)
Gilan	1.01 (0.33-4.29)	0.12 (0.03-0.55)	0.89 (0.29-3.76)	8.91 (4.44-11.48)	1.64 (0.73-2.64)	7.26 (3.64-9.17)	7.51 (4.24-9.99)	1.53 (0.77-2.39)	5.97 (3.43-7.82)	6.38 (0.25-24.92)	11.22 (0.88-44.89)	5.70 (0.14-22.64)
Golestan	1.24 (0.45-4.68)	0.11 (0.03-0.46)	1.12 (0.42-4.26)	11.52 (5.37-14.41)	1.64 (0.70-2.49)	9.88 (4.65-12.13)	10.14 (4.99-13.19)	1.60 (0.75-2.42)	8.54 (4.20-10.99)	7.17 (0.27-24.80)	13.24 (1.18-46.01)	6.56 (0.19-22.52)
Hamadan	1.71 (0.87-4.97)	0.16 (0.06-0.51)	1.55 (0.79-4.45)	11.72 (4.35-15.40)	1.79 (0.58-2.98)	9.93 (3.62-12.77)	10.54 (4.14-14.32)	1.80 (0.61-2.91)	8.74 (3.35-11.64)	5.13 (-0.016-13.29)	9.94 (0.67-24.90)	4.62 (-0.09-11.98)

Hormozgan	2.09 (1.18-5.17)	0.16 (0.07-0.48)	1.92 (1.10-4.71)	8.30 (4.27-10.46)	1.13 (0.53-1.69)	7.17 (3.65-9.10)	7.32 (3.86-9.49)	1.17 (0.56-1.78)	6.14 (3.28-7.94)	2.50 (-0.107-6.184)	6.15 (0.69-14.35)	2.19 (-0.19-5.51)
Ilam	0.45 (0.06-2.43)	0.04 (0.00-0.26)	0.41 (0.06-2.20)	8.04 (5.03-9.89)	1.35 (0.74-2.10)	6.68 (4.19-8.08)	6.48 (4.52-8.02)	1.21 (0.74-1.84)	5.26 (3.68-6.53)	13.14 (1.12-99.94)	24.71 (3.08-205.32)	11.81 (1.01-88.44)
Isfahan	0.99 (0.36-3.84)	0.06 (0.03-0.48)	0.87 (0.32-3.37)	9.26 (3.92-11.94)	1.67 (0.62-2.73)	7.58 (3.27-9.67)	7.71 (3.73-10.10)	1.55 (0.65-2.54)	6.15 (3.03-7.96)	6.72 (0.26-23.49)	11.82 (1.01-42.16)	6.02 (0.16-21.37)
Kerman	0.73 (0.16-3.54)	0.10 (0.01-0.35)	0.66 (0.14-3.20)	10.70 (4.36-14.20)	1.64 (0.57-2.69)	9.05 (3.73-11.99)	8.58 (4.07-11.32)	1.43 (0.59-2.28)	7.14 (3.48-9.53)	10.70 (0.43-61.50)	19.94 (1.44-118.11)	9.74(0.31-55.61)
Kermanshah	1.16 (0.41-4.65)	0.05 (0.02-0.45)	1.05 (0.37-4.17)	11.46 (4.56-15.13)	1.82 (0.66-2.96)	9.64 (3.86-12.39)	9.74 (4.29-13.11)	1.72 (0.69-2.77)	8.02 (3.55-10.54)	7.36 (0.107-26.72)	14.91 (1.00-55.79)	6.58 (-0.00-24.38)
Khorasan-e-Razavi	0.59 (00.9-3.11)	0.91 (0.00-0.26)	0.54 (0.09-2.84)	8.58 (4.74-10.70)	1.22 (0.57-1.95)	7.36 (4.07-9.11)	6.85 (4.35-8.78)	1.13 (0.63-1.84)	5.71 (3.65-7.17)	10.52 (0.61-78.8)	21.57 (1.98-165.03)	9.49 (0.48-71.41)
Khuzestan	8.79 (4.69-12.41)	0.67 (0.39-1.56)	7.88 (4.24-11.07)	12.02 (4.57-15.65)	1.97 (0.66-3.12)	10.04 (3.88-12.82)	11.45 (4.35-15.65)	2.12 (0.69-3.53)	9.33 (3.64-12.54)	0.30 (-0.17-0.90)	1.31 (0.40-2.61)	0.18 (-0.24-0.62)
Kohgiluyeh and Boyer-Ahmad	6.61 (3.71-8.63)	0.07 (0.35-1.97)	5.93 (3.30-7.78)	10.24 (4.14-13.18)	1.92 (0.713.09)	8.31 (3.42-10.52)	9.60 (3.98-12.62)	2.05 (0.78-3.16)	7.55 (3.18-9.94)	0.45 (-0.06-1.04)	2.06 (0.78-3.82)	0.27 (-0.18-0.76)
Kurdistan	0.89 (027-3.72)	1.16 (0.02-0.35)	0.81 (0.25-3.44)	7.94 (4.08-9.96)	1.21 (0.56-1.92)	6.73 (3.46-8.49)	6.62 (3.62-8.66)	1.16 (0.58-1.83)	5.45 (3.00-6.98)	6.36 (0.17-26.52)	13.63 (1.27-55.93)	5.66 (0.07-23.99)
Lorestan	12.29 (4.057.46)	0.07 (0.35-1.97)	11.12 (3.68-15.63)	16.43 (4.01-22.16)	2.86 (0.62-4.77)	13.57 (3.35-17.66)	15.01 (3.70-20.96)	3.03 (0.68-5.20)	11.98 (2.95-16.40)	0.22 (-0.23-0.64)	1.60 (0.57-2.79)	0.07 (-0.31-0.43)
Markazi	0.75 (0.18-3.59)	0.88 (0.01-0.37)	0.68 (0.16-3.20)	10.56 (3.91-14.17)	1.78 (0.58-2.69)	8.77 (3.22-11.54)	8.60 (3.70-11.61)	1.61 (0.59-2.64)	6.98 (2.98-9.25)	10.37 (0.27-56.38)	20.17 (1.20-110.88)	9.27 (0.17-50.54)
Mazandaran	7.19 (4.18-9.68)	0.64 (0.43-1.41)	6.31 (3.68-8.40)	9.51 (4.38-12.28)	1.83 (0.73-2.90)	7.67 (3.55-9.68)	8.89 (4.00-11.89)	1.87 (0.80-2.96)	7.02 (3.22-9.14)	0.23 (-0.12-0.71)	1.12 (0.34-2.19)	0.11 (-0.21-0.56)
North Khorasan	8.51 (4.88-11.38)	0.23 (0.31-1.02)	7.86 (4.51-10.47)	11.91 (4.74-15.21)	1.66 (0.58-2.88)	10.24 (4.10-12.95)	11.08 (4.25-14.43)	1.77 (0.61-2.93)	9.30 (3.69-12.16)	0.30 (-0.17-0.78)	1.75 (0.58-3.36)	0.18 (-0.24-0.62)
Qazvin	2.37 (1.42-5.21)	1.05 (0.11-0.55)	2.13 (1.28-4.65)	9.30 (4.25-12.01)	1.52 (0.57-2.45)	7.78 (3.55-9.88)	7.97 (3.87-10.60)	1.51 (0.62-2.46)	6.46 (3.23-8.52)	2.35 (-0.11-5.50)	5.32 (0.52-12.51)	2.02 (-0.19-4.83)
Qom	11.41 (4.55-16.07)	0.05 (0.38-1.81)	10.36 (4.05-14.43)	12.06 (3.69-15.86)	2.00 (0.53-3.24)	10.06 (3.08-13.14)	11.70 (3.58-16.09)	2.20 (0.62-3.67)	9.50 (2.97-12.76)	0.02 (-0.31-0.26)	1.09 (0.35-2.11)	-0.08 (-0.37-0.22)
Semnan	0.57 (0.11-2.99)	0.04 (0.00-0.32)	0.52 (0.10-2.65)	8.54 (4.10-11.08)	1.35 (0.60-2.22)	7.19 (3.46-9.15)	6.34 (3.47-8.44)	1.12 (0.57-1.76)	5.21 (2.87-7.02)	9.95 (0.46-66.62)	18.36 (1.60-124.60)	9.01 (0.33-61.32)
Sistan and Baluchistan	0.64 (0.14-3.11)	0.65 (0.00-0.22)	0.60 (0.13-2.88)	14.03 (4.57-18.57)	1.52 (0.47-2.49)	12.50 (4.09-16.28)	11.73 (4.38-15.87)	1.47 (0.53-2.46)	10.26 (3.79-13.88)	17.13 (-0.18-0.78)	31.36 (2.05-177.70)	16.05 (0.63-88.83)
South Khorasan	8.24 (3.54-11.42)	1.54 (0.25-1.10)	7.58 (3.26-10.57)	11.37 (3.63-14.77)	1.70 (0.49-2.79)	9.67 (3.01-12.27)	10.67 (3.31-14.43)	1.82 (0.51-2.97)	8.85 (2.79-11.88)	0.29 (-0.18-0.78)	1.79 (0.58-3.16)	0.16 (0.63-88.83)
Tehran	12.40 (3.64-11.42)	0.05 (0.39-2.68)	10.86 (3.25-15.35)	12.10 (3.75-16.47)	2.39 (0.66-3.96)	9.71 (3.01-13.00)	11.25 (3.45-15.68)	2.46 (0.68-4.11)	8.78 (2.71-12.06)	-0.09 (-0.31-0.26)	0.59 (0.11-1.40)	-0.19 (-0.39-0.11)
West Azarbayejan	0.58 (0.10-3.03)	0.07 (0.00-0.28)	0.53 (0.09-2.76)	8.66 (4.58-10.96)	1.29 (0.56-1.96)	7.37 (3.92-9.14)	7.07 (4.27-9.47)	1.20 (0.63-1.86)	5.86 (3.59-7.43)	11.00 (0.75-79.63)	21.75 (2.15-158.55)	9.94 (0.59-72.13)
Yazd	0.66 (0.13-3.25)	0.05 (0.01-0.36)	0.59 (0.12-2.89)	9.26 (4.02-12.19)	1.53 (0.58-2.52)	7.72 (3.42-9.99)	7.10 (3.66-9.42)	1.33 (0.59-2.10)	5.77 (3.00-7.50)	9.63 (0.41-57.94)	17.83 (1.38-110.56)	8.66 (0.29-51.87)
Zanjan	0.46 (0.07-2.48)	0.06 (0.00-0.29)	0.41 (0.06-2.23)	6.73 (3.76-8.32)	1.10 (0.55-1.76)	5.62 (3.22-6.88)	5.45 (3.48-6.94)	1.00 (0.56-1.54)	4.45 (2.89-5.59)	10.67 (0.83-76.75)	18.83 (1.97-142.30)	9.68 (0.70-70.75)
IRAN	4.43 (3.09-5.41)	0.50 (0.29-0.74)	3.93 (2.78-4.72)	10.54 (4.37-13.02)	1.79 (0.67-2.76)	8.75 (3.65-10.57)	۹,۲۵ (-۱۱,۵۰ ۴,۱۰)	1.7۷ (0.70-2.76)	7.48 (3.34-9.05)	1.08 (0.17-1.72)	2.53 (1.07-3.86)	0.90 (0.06-1.45)

As shown in Table 3, Iran's Disability-Adjusted Life Years (DALYs) indicate significant changes from 1990 to 2021. This disease burden consists of two main components, Years Lived with a Disability (YLDs) and Years of Life Lost due to premature death (YLLs). Since 1990, the burden of thyroid cancer in Iran has been, on average, 4.44 (95% CI: 3.09-4.41). In 1995, this value changed to 4.43 (95% CI: 3.10-5.31), and in 2000, the burden of the disease changed to 4.20 (95% CI: 2.92-4.92). This value rose in 2010 to 8.71 [%95 CI: 8.71 (4.36-10.41)], declined in 2015 to 10.54, and finally dropped in 2021 to [%95 CI: 9.25 (4.25-11.50)] (Fig.5)

YLDs were [%95 CI: 0.50 (0.29-0.74)] in 1990; they increased to [%95 CI: 1.79 (0.67-2.67)] in 2015 but diminished to [%95 CI: 1.08 (0.17-1.72)] in 2021. YLLs were [%95 CI: 3.93 (2.78-4.72)] in 1990, rising to [%95 CI: 8.75 (3.65-10.57)] in 2015, then falling to [%95 CI: 7.48 (3.34-9.05)] in 2021.

Annual average percentage change (AAPC): The annual average percentage change (AAPC) has been positive in some regions and negative in others. For instance, in provinces such as Bushehr, AAPC has reached 14.93%, Chahar Mahaal and Bakhtiari +10.04, Ilam +13.04, Sistan and Baluchistan +17.13, and Zanjan +10.67, indicating a significant rise in the burden of disease. There has been no substantial increase in some provinces, and in some provinces, including Alborz, Ardebil, Kurdistan, Mazandaran, Lorestan, and South Khorasan, these changes (AAPC) have had a downward trend. Overall, the burden of thyroid cancer in Iran has grown from 1990 to 2021. These changes can help policymakers and researchers better understand prevalence patterns and health needs, as well as design more effective plans to control and prevent this disease.

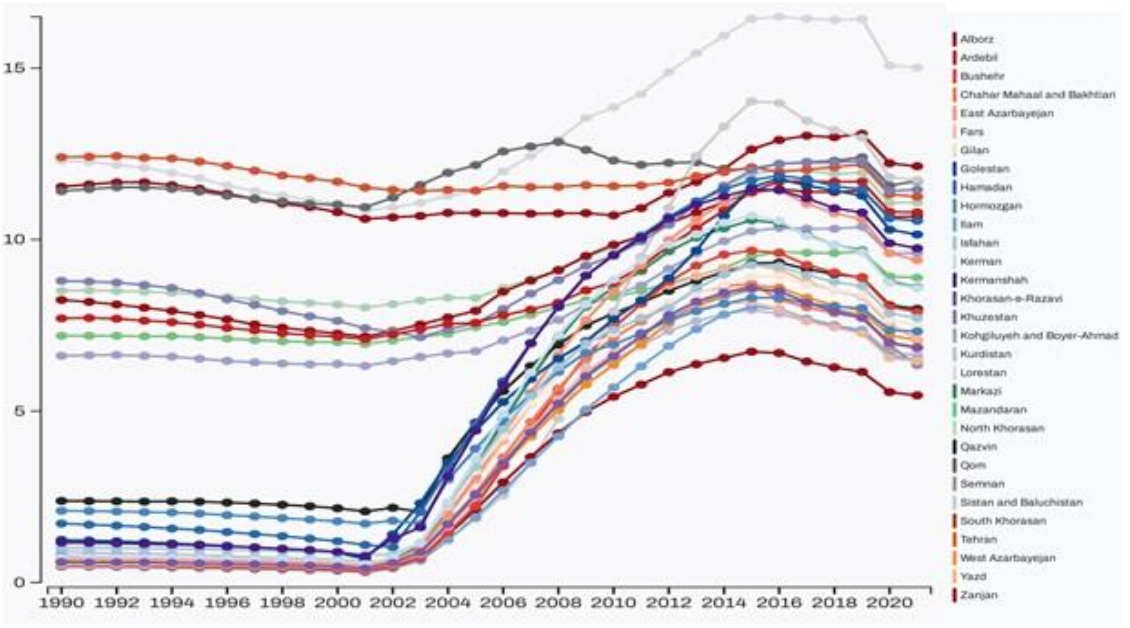


Fig. 5. The trend of Disability-Adjusted Life-Years (DALYs) rate of thyroid cancer in the Iranian population from 1990 to 2021

According to the results shown in Table 4, the Human Development Index (HDI) and its components positively affect the incidence of thyroid cancer. Specifically, as the index increases, so does the disease incidence, and this relationship is statistically significant ($P < 0.005$).

Table 4. Thyroid cancer incidence and human development index (HDI) in Iran 1990-2021

Incidence	Coefficient	Std. err	T	P-Value	Conf. interval [95%]	
HDI	-306.2484	76.97068	-3.98	0.000	-464.4639	-148.0329
Life expectancy	1.678305	0.3494105	4.80	0.000	0.9600811	2.396528
Expected years of schooling	3.341781	0.7578933	4.41	0.000	1.783909	4.899653
Mean years of schooling	3.769234	1.041182	3.62	0.001	1.629054	5.909413
Gross national income per capita for every 1000 people	15.04357	3.851539	3.91	0.001	7.126618	22.96052
-Cons	-115.0529	24.32115	-4.73	0.000	-165.0457	-65.06005

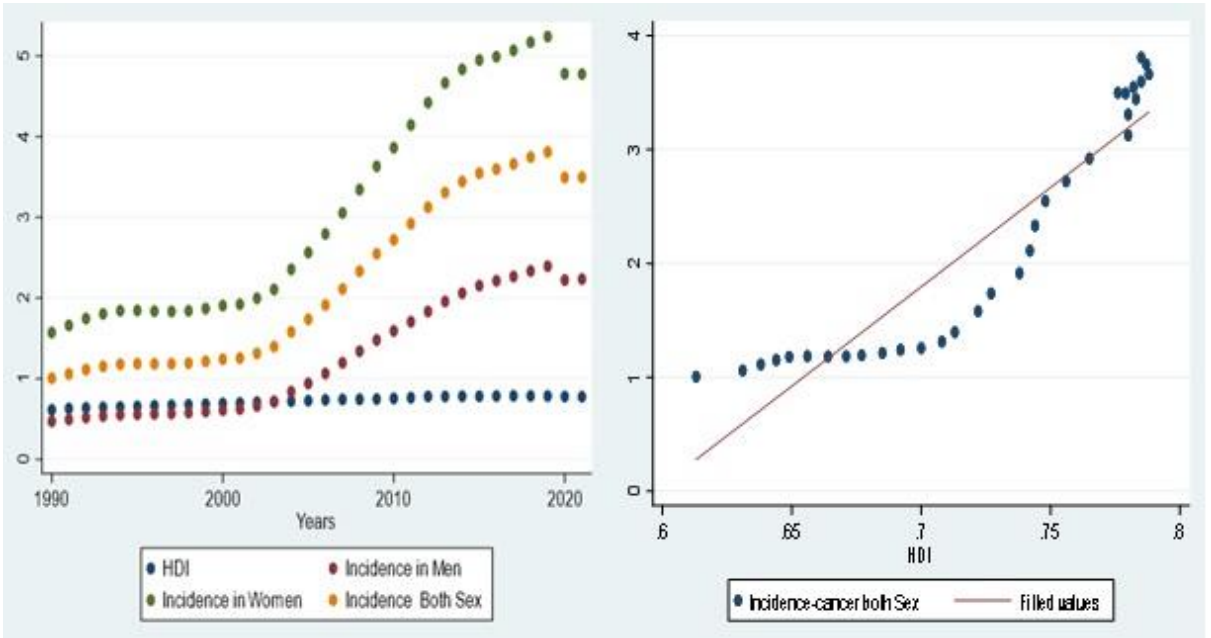


Fig. 6. Relationship between the Human Development Index and the incidence of thyroid cancer from 1990 to 2021

Fig. 6. indicates that there is a direct relationship between the Human Development Index (HDI) and the incidence of thyroid cancer in women, men, as well as the adjusted incidence in both sexes (women and men); with an increase in the Human Development Index, the incidence of this disease has also risen. In general, the incidence, prevalence, and burden of thyroid cancer diseases in most provinces of Iran have had an upward trend along the years 1990 to 2020 and a relatively diminishing trend in 2021. The declining trend in thyroid cancer disease burden (DALYs) as well as incidence and prevalence rates in Iran in 2021 may have been influenced by several factors, including the COVID-19 pandemic. The COVID-19 pandemic has led to disruptions in healthcare services, and many patients may have avoided visiting healthcare centers owing to restrictions and fear of being infected with the virus. This could lead to a decline in new thyroid cancer diagnoses, thereby lowering the disease burden. Also, during the COVID-19 pandemic, attention and resources have been directed towards controlling and treating COVID-19; this may have affected cancer screening and treatment programs.

Discussion

This study aimed to examine the incidence, mortality, disability-adjusted life years (DALYs), years of life lost due to mortality (YLL), and years lived with a disability (YLDs) related to thyroid cancer, as along with the relationship between this disease and the Human Development Index (HDI). The results indicated that the overall burden of thyroid cancer has significantly grown in Iran from 1990 to 2021, with variations observed across different Iranian provinces.

In recent years, the incidence of thyroid cancer in Iran has increased, possibly due to improved access to diagnostic services and a rise in specific risk factors. An investigation into the relationship between this disease and the Human Development Index (HDI) indicates that factors influencing human development, such as national income, life expectancy, and years of education, significantly affect the prevalence and early diagnosis of thyroid cancer [16, 17]. The results of this study and other studies on the relationship between the incidence of some cancers and HDI reveal that as HDI increases, so does the likelihood of thyroid cancer increases [17]. In particular, the positive relationship between life expectancy as well as years of education and the incidence of this disease could be due to greater access to health information and services. These results highlight the importance of ameliorating the quality of life and education levels in reducing diseases [15-17]. Further, the decline in YLL in provinces, including Tehran, from 1990 to 2021, may be due to inequalities in thyroid cancer treatment and inequity in the quality of health care in Tehran compared to other cities across Iran [18].

Note that the observed trend in incidence, burden of thyroid cancer, years of life with disability, and years of life lost due to premature death had an upward trend from 1990 to 2021 [19]. The observed pattern and growing trend in thyroid cancer incidence may be owing to several factors. Improvements have occurred in medical techniques in diagnosis and may have led to a higher incidence of much lower-stage malignancies, thus resulting in over-diagnosis [20]. It is also estimated that countries including South Korea, Belarus, China, Italy, Croatia, Slovakia, and France between 2008 and 2012 account for more than 80% of thyroid cancer in women [21].

Similarly, in Spain, the increase in thyroid cancer incidence is mainly attributed to overdiagnosis. Nevertheless, compared to global rates, the rise in thyroid cancer incidence in Iran was relatively low [22, 23]. This could also be explained by Iran's relatively low rate of overdiagnosis. Even though the increase in

AAPC and DALYs in other countries, including South Korea (24), has been primarily due to elevated diagnosis rates by cancer screening programs, this scenario does not apply to Iran since there is currently no thyroid cancer screening program in Iran. Given the significant differences in rates, including incidence and DALYs, in other regions, thyroid cancer screening programs will likely be cost-effective in different areas [25, 26].

Further studies are required to more accurately ascertain the role of these factors in the increasing burden of thyroid cancer in Iran. Note that despite the rising incidence, the minor difference in mortality rates between 1990 and 2021 may be owing to better clinical management of thyroid cancer in recent years [27].

Nevertheless, despite its apparent success, the Iranian healthcare system is currently facing new challenges in the field of non-communicable diseases [28] This may also affect the management of these diseases, including thyroid cancer. Thus, a more detailed analysis at the subnational level using quality of care indicators needs to be conducted in Iran [29]. As the results of our study revealed, the incidence of thyroid cancer is about 3 times higher in women than in men. Although the reason for the higher burden of thyroid cancer in women remains unknown, there are possible explanations. One explanation is that there are similar hormonal signaling pathways involved in thyroid and breast cancer, both of which have the highest incidence in women [30].

The results of this study are in accordance with those of the World Health Organization's warning about thyroid cancer worldwide [31]. 0.049% (0.044–0.053) of all DALYs in 2019 were due to thyroid cancer, yet only 0.003% of the global cancer research budget is allocated to thyroid cancer. Therefore, the allocation of resources for thyroid cancer research, management, and improvement of healthcare quality may need to be reconsidered at a global level [32]. Also, the lack of adherence to health standards and decline in lifestyle improvements worldwide are increasing risk factors; they may increase the incidence of thyroid cancer [33].

This study, along with similar studies, will help allocate appropriate resources to health systems for managing the burden of thyroid cancer and reduce inequalities in access, diagnosis, and treatment. Furthermore, exposure to risk factors for this cancer, including exposure to chemicals, unhealthy lifestyles, and other factors mentioned above, should be mitigated as much as possible.

One of the main limitations was the lack of accurate and comprehensive data at the local level, particularly in rural and less developed areas, where the incidence of thyroid cancer may not be accurately recorded. Further, changes in disease classification and diagnostic methods over time can be influential; inconsistencies or incorrect data comparisons may lower the accuracy of this study.

Conclusion

As thyroid cancer can impose a financial and emotional burden on families, it is essential to determine the trend of cancer in different regions of the world before initiating preventive measures. Comparing the trend and geographical distribution of cancer helps us identify areas with high disease rates. It can also provide an opportunity to appraise the impact of screening programs. Eventually, new strategies should be adopted to prevent the disease if an increasing trend is observed.

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Conflict of interest

None declared.

Funding

None.

Ethical Considerations

Data for this study were derived from the Global Burden of Disease (GBD) database. As the analysis was based solely on secondary data sources, no direct involvement of patients or human participants was required.

Code of Ethics

This study received approval from the ethics committee of Bam University of Medical Sciences, with the ethics code IR.MUBAM.REC.1404.002.

Authors' Contributions

Victoria Momenabadi: Conceptualization, methodology, investigation, writing original draft, review, and editing; Fatemeh Doost Mohammadi: Investigation, writing original draft, review, and editing; Fatemeh Saeedinezhad: Project administration, data curation, investigation, writing—original draft, review, and editing; Nima Ghazal: Methodology, writing review, and editing; Ali Karampour: Writing original draft, review, and editing; Mojang Navabi: Conceptualization, methodology, investigation, supervision, project administration, data curation, writing original draft, review, and editing; Behrooz Alipouryan Motlagh: Project administration, writing original draft, review, and editing; Zaher Khazaei: Conceptualization, methodology, investigation, writing original draft, review, and editing.

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