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Geographic Variation and Trends in Laryngeal Cancer Incidence in Iran: A Comprehensive Analysis

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ABSTRACT

Background and Aims: Laryngeal cancer poses a significant health challenge, particularly in Iran, where it exerts a substantial burden on the healthcare system. This study aimed to comprehensively analyze the geographic variation in laryngeal cancer incidence across Iran, estimate its burden in 2022, and project trends up to 2050.

Methods: Our study utilized data from two sources: the Iran National Population-based Cancer Registry (INPCR) for a four-year period (2014-2017) and the GLOBOCAN 2022 study. From the INPCR data, we calculated average age-standardized incidence rates (ASIRs) for each province. Additionally, the GLOBOCAN 2022 study provided estimates of laryngeal cancer incidence and mortality rates for 2022, along with projections for future trends until 2050.

Results: Laryngeal cancer displayed significant regional variations within Iran between 2014 and 2017, with Kerman and North Khorasan provinces experiencing the highest incidence rates. Laryngeal cancer incidence increased with age and remained considerably higher in males. In 2022, laryngeal cancer represented 2 % of new cancer cases in Iran, with ASIRs higher than global averages. By 2050, a substantial increase in both incidence and mortality rates is projected, emphasizing the growing burden of laryngeal cancer in Iran.

Conclusion: This study highlights the substantial variations in laryngeal cancer incidence across Iranian provinces. Our findings suggest that opium use, in addition to established risk factors like tobacco and alcohol, might contribute to the high incidence rates observed in Iran. Early diagnosis and targeted interventions tailored to regional risk factor prevalence are crucial to address the growing public health burden of laryngeal cancer in Iran.

Keywords: Laryngeal cancer, Geographic variation, Incidence, Mortality, Projection, Iran

INTRODUCTION:

Laryngeal cancer is a significant global health issue, representing around 30-40% of malignant head and neck tumors and 1%-2.5% of all cancer cases (1). It is estimated to be the 20th most common cancer worldwide, with over 189,000 new cases annually. In 2022, there were 165,794 cases in males and 23,397 cases in females (2). It has a non-uniform geographical distribution, with varied incidence and mortality rates across different regions (3). The highest age-standardized incidence rates (ASIR) of laryngeal cancer were recorded in Cuba for men (16.6 per 100000) and women (2.3 per 100000) (2). Over the past 3 decades, despite the global decrease in ASIR of laryngeal cancer, East Asia, the Caribbean, and Oceania were the three regions that experienced substantial rises in ASIR (4).

Laryngeal cancer is more prevalent in males than in females and usually manifests beyond the age of 65 (5). Various environmental, social, and behavioral factors impact this unequal distribution (6). Regional differences in risk factors such as tobacco and alcohol intake, as well as opium usage, affect the prevalence of laryngeal cancer (7–9). Laryngeal cancer in Iran exhibits a distinct epidemiological profile, which has attracted considerable attention in research.

Understanding these geographic variations and their potential contributing factors is crucial for customizing efficient prevention and diagnostic approaches tailored to the unique needs of Iranian provinces (10). Yet, there is a lack of thorough research on the geographic variations of laryngeal cancer in this area, and existing data may show inconsistencies in provincial details and ASIR. This study aims to provide a thorough examination of the geographic variations in laryngeal cancer incidence throughout Iran. We calculated the burden of laryngeal cancer in Iran for 2022 and forecasted future trends till 2050. The findings provide significant information for policymakers and planners to allocate resources, establish screening programs, and develop treatment plans customized to the unique requirements of several provinces in Iran.

Sources and Methods:

Data was collected from two sources: the Iran National Population-based Cancer Registry (INPCR) and Global Cancer Statistics (GLOBOCAN) 2022. Established in 2014 by the Iranian Ministry of Health and Medical Education (MOHME), INPCR provides high-quality cancer incidence data for nearly 80 million people in Iran. The INPCR database adheres to the International Association of Cancer Registries (IACR) guidelines and employs the third edition of the International Classification of Diseases for Oncology (ICD-O-3) for data collection and tumor characteristics coding (11).

Provincial incidence data were acquired from INPCR for all 31 provinces of Iran over the first four years of INPCR data collection, spanning from 2014 to 2017. Using the World Health Organization standard population, we calculated the average ASIR of Laryngeal cancer per 100,000 person-years from 2014 to 2017 for each province, categorized by gender. We reported numbers, percent, crude incidence rates, age-specific incidence rates, and ASIR at provincial and national levels. Data were analyzed using Microsoft Excel for descriptive statistics and R software for thematic mapping.

Furthermore, estimations for the year 2022 and projections until 2050 were obtained from GLOBOCAN 2022, a project administered by the International Agency for Research on Cancer (IARC). These estimations include ASIR and age-standardized mortality rates (ASMR) per 100,000 person-years and 5-year prevalence of laryngeal cancer among the Iranian male and female population. Globocan 2022 is based on the 1966 Segi-Doll World standard population, and the estimations for all 36 cancer types are based on codes from the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10). The sources and methods employed in GLOBOCAN 2022 estimations are described on the Global Cancer Observatory (GCO) website (2). The estimation methods are country-specific, and the quality of the national estimates depends on the coverage, accuracy, and timeliness of the recorded incidence and mortality data in a given country.

For Iran, The GLOBOCAN 2022 estimated the incidence

by calculating the weighted average of rates from Ardabil Province, Golestan Province, and East Azerbaijan between 2004 and 2017. This estimate was then projected to 2022 and applied to the population of 2022. Death rates from 2013 to 2016 were used to estimate mortality in the 2022 population (12).

Result:

Geographic distribution of laryngeal cancer in Iran

Table 1 comprehensively summarizes laryngeal cancer incidence rates, including numbers, ASIRs and crude rates, stratified by sex and province. A total of 6,900 cases of laryngeal cancer were recorded during this period. We found a notable regional disparity in laryngeal cancer incidence rates across Iran. Among Iranian males, Kerman and North-Khorasan provinces reported the highest average ASIRs, with rates of 9.88 and 6.95 per 100,000, respectively. In contrast, the lowest average ASIR in males was documented in Zanjan) 1.84 per 100,000(. For females, North-Khorasan and South-Khorasan provinces had the highest average incidence rates, with ASIRs of 2.12 and 2.03 per 100,000, respectively. Conversely, Kohgiluyeh-va-Boyerahmad province had the lowest average ASIR among females, at 0.08 per 100,000.

The geographic distribution of laryngeal cancer incidence in Iran between 2014 and 2017 is also visualized in Figure 1. The highest incidence rates were observed in the southeastern and northeastern provinces. Conversely, the southwestern regions of Iran exhibited the lowest incidence rates of laryngeal cancer.

Figure 2 illustrates the age-sex-specific patterns of laryngeal cancer incidence. The pyramid-like representation of the data reveals a substantial increase in laryngeal cancer incidence with advancing age. Notably, individuals aged 50 years or older exhibited the highest incidence rates. In males, the age group of 80-84 years recorded the highest ASIR for laryngeal cancer, reaching 33.48 per 100,000 person-years. For females, the age group exceeding 85 exhibited the highest ASIR, with a rate of 10.01 per 100,000 person-years. Laryngeal cancer incidence was consistently higher in males than in females across all age groups.

National Laryngeal cancer burden

Laryngeal cancer accounted for 2.0% of all new cancer cases in Iran in 2022. According to the GLOBOCAN 2022, there were 2,762 new cases of laryngeal cancer in Iran, with ASIRs of 5.0 per 100000 for males and 1.1 per 100000 for females. These rates were 1.4 and 2.4 times higher than the global averages. In the same year, Iran recorded 1,874 deaths attributed to laryngeal cancer. The ASMR for males and females were 3.1 per 100000 and 1.1 per 100000, respectively, which exceeded the global figures by 1.6 and 4.7 times, respectively. The 5-year prevalence of this cancer in 2022 was 9,092, comprising 7,505 males and 1,587 females (Table 2).

projection of incidence and mortality to 2050

GLOBOCAN has provided projections for future cancer incidence and mortality burden from 2022 to 2050. These estimations indicate a concerning trend of increasing incidence and mortality rates for laryngeal cancer over the next 3 decades, in Iran. Specifically, between 2022 and 2050, the number of new cases is expected to rise by 137.3 % (from 2,762 to 6,554 cases), with a 130.3 % increase in males (from 2,259 to 5,203 cases) and a 168.4 % increase in females (from 503 to 1,350 cases; Fig 3). Concurrently, the estimated number of deaths due to laryngeal cancer for both sexes increased by 189.9 % (from 1,874 to 5,432 deaths). Over the same decade, this reflects a 165.5 % increase in males (from 1,400 to 3,717 deaths) and a 261.8 % increase in females (from 474 to 1,715 deaths; Fig 3).

Discussion:

Our findings revealed significant geographical variations in laryngeal cancer incidence across Iranian provinces. Additionally, the incidence rates consistently increased with age and were notably higher in men compared to women across all age groups. In 2022, Iran's burden of laryngeal cancer, as measured by ASIR, ASMR, and 5-year prevalence, significantly surpassed global estimates for both sexes. These rates were 1.57, 2.1, and 1.43 times higher than the global average, respectively. Even more concerning, these already

Table 1. The average laryngeal cancer statistics in Iran between 2014-2017, according to sex and province

		male			female			Population of province
	Province	Number	Crude	ASIR	Number	Crude	ASIR	
1	Alborz	43	3.15	3.56	5	0.38	0.41	2,712,400
2	Ardabil	17	2.62	3.15	4	0.56	0.57	1,270,420
3	WestAzar	64	3.87	4.81	13	0.79	0.86	3,265,219
4	EastAzar	79	4.01	4.09	15	0.78	0.73	3,909,652
5	Bushehr	12	1.87	2.97	4	0.69	0.96	1,163,400
6	Charmahal	13	2.67	3.45	1	0.27	0.26	947,763
7	Fars	101	4.13	4.53	11	0.44	0.46	4,851,274
8	Ghazvin	19	2.95	3.35	6	0.93	1.02	1,273,761
9	Gilan	62	4.88	3.95	5	0.39	0.28	2,530,696
10	Golestan	32	3.42	4.45	12	1.23	1.45	1,868,819
11	Hamadan	38	4.28	4.37	3	0.34	0.31	1,738,234
12	Hormozgan	16	1.76	2.63	5	0.52	0.79	1,776,415
13	Ilam	7	2.37	2.57	2	0.61	0.72	580,158
14	Kerman	118	7.41	9.88	15	0.96	1.15	3,164,718
15	Kermanshah	32	3.26	3.43	18	1.81	1.61	1,952,434
16	Khorasan Jonoubi	16	4.11	4.76	8	2.03	2.03	768,898
17	khorsan-razavi	115	3.59	4.43	32	1.00	1.15	6,434,501
18	Khorasan-Shomali	26	5.81	6.95	8	1.82	2.12	863,092
19	Khuzestan	66	2.74	3.74	7	0.31	0.42	4,710,509
20	Kohgiloye-Boirahmad	7	1.90	2.63	0	0.07	0.08	713,052
21	Kurdistan	25	3.14	3.58	4	0.54	0.58	1,603,011
22	Lorestan	28	3.14	3.72	2	0.19	0.19	1,760,649
23	Markazi	29	3.92	4.31	3	0.46	0.39	1,429,475
24	Mazandaran	72	4.39	4.01	11	0.67	0.58	3,283,582
25	Semanan	16	4.43	4.53	3	0.98	1.00	702,360
26	Systan-Baluchestan	17	1.20	2.50	5	0.36	0.68	2,775,014
27	Tehran	282	4.30	4.26	28	0.43	0.41	13,267,637
28	Yazd	20	3.55	4.27	2	0.38	0.36	1,138,533
29	Zanjan	8	1.55	1.84	1	0.24	0.24	1,057,461
30	Esfahan	91	3.51	3.49	11	0.43	0.39	5,120,850
31	Ghom	19	2.86	3.62	4	0.68	0.83	1,292,283
	total	1481	3.72	4.19	244	0.63	0.65	79,926,270

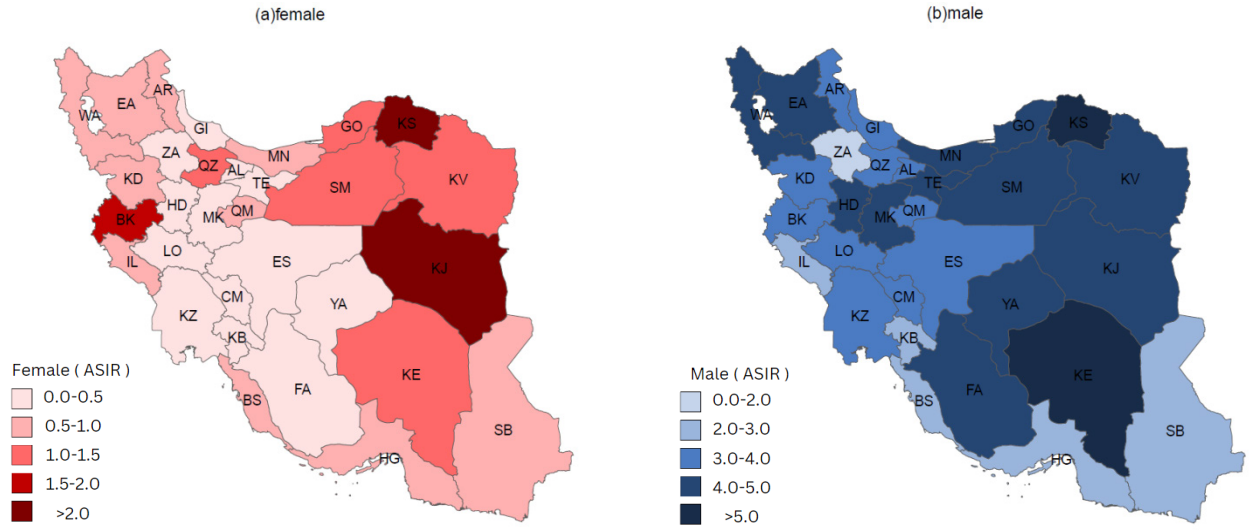

Figure 1. The geographic distribution of the average age-standardized rate of laryngeal cancer incidence in Iran between 2014-2017 by sex.

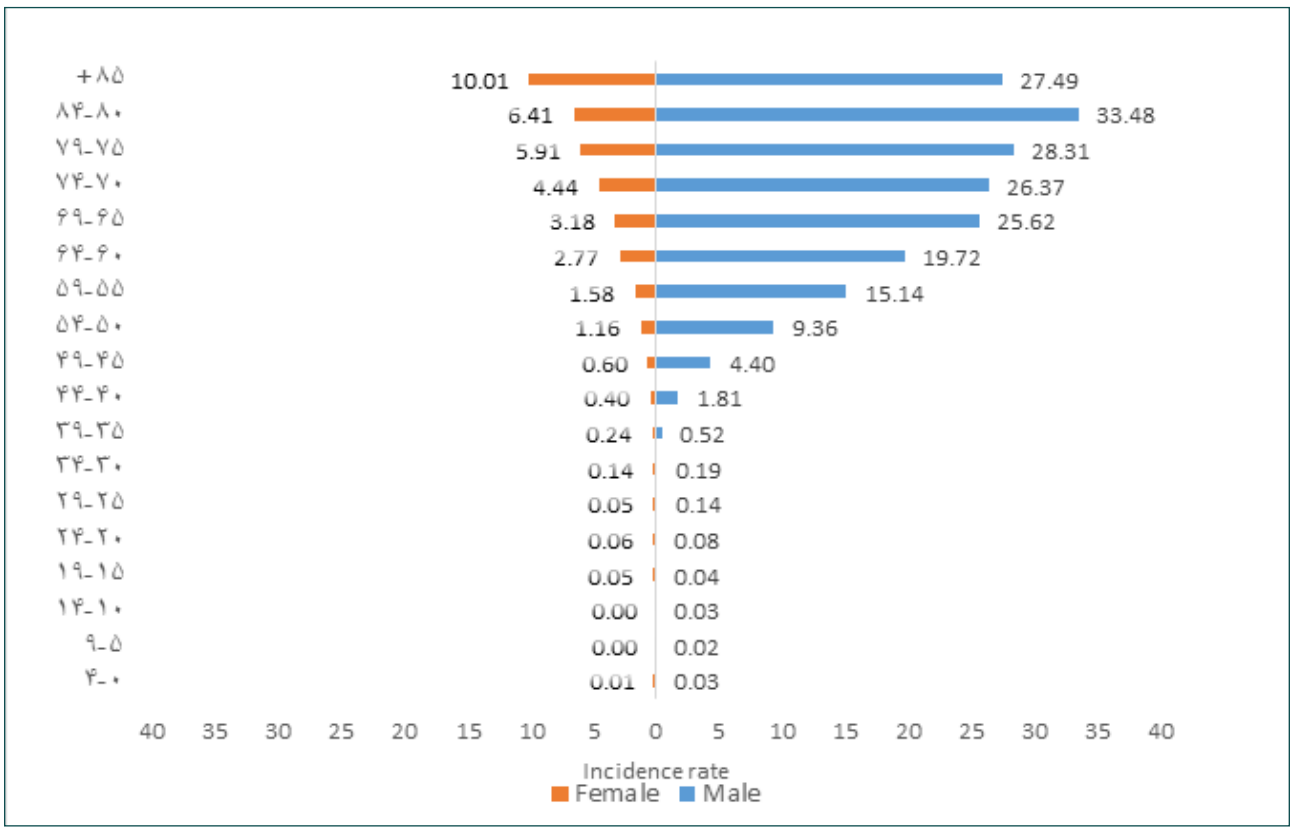

Figure 2. The average age-standardized rates of laryngeal cancer incidence in Iran between 2014-2017 by age group and sex.

Table 2. Comparison of age-standardized incidence rate, mortality rate, and 5-year prevalence of laryngeal cancer in Iran with global trend in 2022

	Incidence (ASIR)			Mortality (ASMR)			5-year prevalence number (Rate)		
	Male	Female	Both	Male	Female	Both	Male	Female	Both
Iran 2022	5.0	1.1	3.0	3.1	1.1	2.1	7,505 (17.3)	1,587 (3.7)	9,092 (10.6)
World 2022	3.5	0.45	1.9	1.9	0.23	1.0	514,135 (12.9)	69,733 (1.8)	583 868 (7.4)

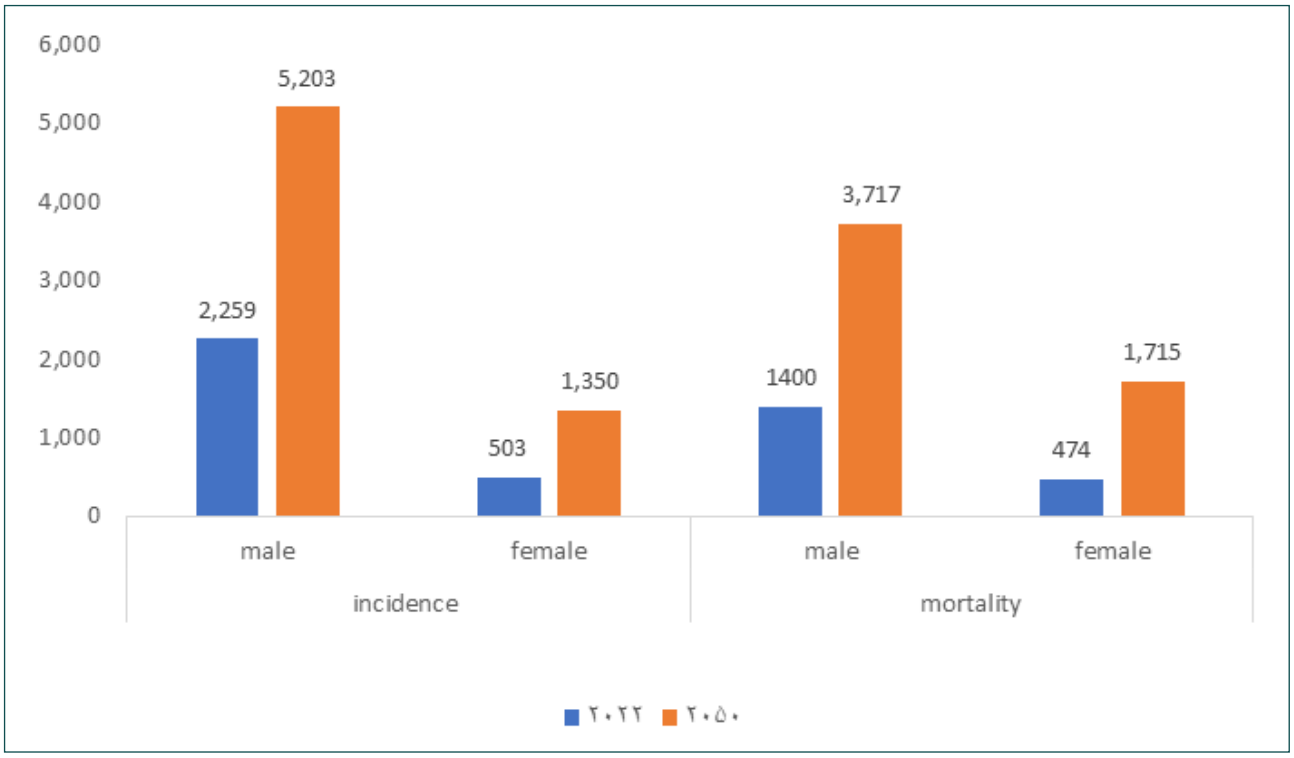

Figure 3. Incidence and mortality number of laryngeal cancer cases by sex for the years 2022 and 2050, in Iran

high rates are projected to continue rising over the next three decades.

Our study identified a significant east-west divide in laryngeal cancer incidence across Iranian provinces. The southeastern and northeastern regions exhibited higher ASIRs compared to the southwestern provinces. This observed geographical disparity aligns with the findings of Roshandel et al. (2019), who reported similar patterns in laryngeal cancer rates among Iranian males in 2014 using INPCR data (13). These variations likely stem from differences in lifestyle and risk factor prevalence across the country. A recently published study in Iran, suggests that it is possible to avoid up to 73.2% of laryngeal cancer cases by removing exposure to its risk factors (14). The most prominent and modifiable risk factors for laryngeal cancer include tobacco, alcohol, and opium consumption (7,8). Depending on how much these risk factors are available in a region, they might be more or less accountable for the laryngeal cancer cases in that region. While the established risk factors of tobacco and alcohol consumption don't appear to fully explain the observed patterns (15,16), opium use, particularly prevalent in southeastern and northeastern provinces bordering Afghanistan, might

be a significant contributing factor in Iran (17,18). Kerman province, with the highest ASIR for laryngeal cancer among Iranian males (9.88 cases per 100,000 individuals), also exhibits a higher prevalence of opium consumption compared to the national average (19).

Socioeconomic status (SES) might also play a role. Several studies have been conducted in the US, Canada, and European countries to investigate the association between SES and head and neck cancers (HNC) (20–24). Research suggests that within the scope of SES factors, those who are single or never married, have lower educational attainment, and experience reduced income levels are more likely to have a higher rate of HNC (25). In Iran, based on Neisi's study, provinces with lower Human Development Index (HDI) scores, encompassing life expectancy, education, and income levels, tend to coincide with areas exhibiting higher laryngeal cancer incidence (26,27). While this observation suggests a potential relationship, further research is necessary to confirm this association in the Iranian context.

Our observations highlight a notable gender disparity in laryngeal cancer incidence rate which is consistent with prior studies. According to the Global Burden of Disease study, incident and death cases of laryngeal cancer were sixfold and fivefold greater in men than in women in 2017 respectively (3). The relationship between sex and laryngeal cancer incidence has been long investigated and can be due to a higher proportion of tobacco smokers, alcohol, and opium consumers among men compared to women (28,29).

Our study revealed an increased incidence of laryngeal cancer among individuals as they age, particularly after reaching the age of 50. This trend aligns with the findings of previous research, which have indicated that the highest incidence of laryngeal cancer typically occurs after the age of 65 for both males and females (5). Furthermore, epidemiological investigations have demonstrated that only 2–10% of laryngeal cancer cases involve individuals younger than 40 years old, a pattern that is consistent with our observations (30).

What's concerning is that both the incidence and mortality rates for laryngeal cancer in Iran are higher than the average global rates for 2022. These rates will continue to rise in Iran over the next three decades, increasing the burden of this cancer. The prevalence of risk factors and most importantly opium use can explain the higher incidence of laryngeal cancer in Iran. Moving beyond incidence, higher mortality rate of laryngeal cancer is associated with its lower 5-year survival rate, which falls below 60 % (31). This might be partially explained by diagnosis delays, studies show that HNCs diagnosed at early stages can have survival rates as high as 80 % (32). One Iranian study found an average patient delay of nearly 3 months (ranging from 1 week to a year), with a professional delay averaging 4.26 weeks (ranging from 1 to 39 weeks) (31). Previous research suggests that professional delays exceeding 12 months significantly impact disease-specific survival (33). More studies are required to precisely determine the diagnosis delay and survival rate in Iran, as well as the probable association between them. Nonetheless, screening is a tool for early diagnosis which might be beneficial for populations deemed high risk for HNCs who are less likely to self-refer. Therefore we believe that regional screening for specific populations with recognizable risk factors such as opium and tobacco use could offer a cost-effective approach (34). Plus, informing the community about the signs and symptoms of laryngeal cancer should be a priority in health politics. Furthermore, One effective method to reduce the mortality rate is to establish a periodic follow-up system, as it directly affects patients who have been diagnosed with cancer (35).

A strength of this study was the utilization of four years of data from INPCR, enhancing the accuracy of our province-level average ASIRs. Moreover, including females in our study broadened its scope and relevance. However, there were certain limitations to our research. we estimated values for Qom province based on three years of data from 2015 to 2017. It's essential to note that this limitation had no noticeable impact on the outcomes at the provincial level.

Conclusion:

In conclusion, our study revealed notable variations in laryngeal cancer rates across different regions and demo-

graphic groups in Iran, with older males exhibiting higher rates. Our research indicates that opium consumption could be an important contributing factor, particularly in areas with a high prevalence. These findings seem to be associated with socioeconomic status, suggesting the need for customized interventions. Furthermore, the increasing incidence of laryngeal cancer highlights the necessity for enhanced screening and awareness programs.

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