



Epidemiological Study of Lung Cancer in Iran: A Systematic Review

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Abstract

Background: There is no comprehensive study addressing all the epidemiological aspects of Lung cancer (LC) in Iran, therefore this systematic review investigated the epidemiological aspects of lung cancer in Iran.

Methods: The search was performed until the Aug. 2020 on the in international databases based on PRISMA protocol by Pulmonary Neoplasms, Lung Neoplasm, Neoplasm, Lung, Lung Cancer, Cancer, Pulmonary Cancer, Cancer, Pulmonary, Cancers, Cancer of the Lung, Iran, incidence, death, risk factors keywords and different combinations of them. Articles that evaluated epidemiological aspects of lung cancer were included in the analysis.

Results: Of 1420 articles, 82 cases were entered the analysis. Based on studies, in Iran, lung cancer has been the most common cancer and its prevalence is increasing. Squamous cell carcinoma and adenocarcinoma is the most common type of lung cancer in men and women, respectively. Cigarette smoking, human papilloma virus (HPV) infection, mustard gas, occupational risk factors and genetic factors considered as the major reported risk factors for lung cancer and vegetarian diet as a protective factor.

Conclusion: In according to the increasing trend of incidence and mortality of lung cancer in Iran, elimination of the major risk factors can decrease this issue and national comprehensive planning should be considered in health promotion plans.

Keywords: Lung cancer; Epidemiology; Risk factor; Survival; Iran

Introduction

Lung cancer (LC) is second most common cancer in both genders and most common and deadliest cancer worldwide, with a 5-year survival rate of 19% and estimated that 13% of cancer incidence and 24% of cancer mortality causes related to lung cancer (1).

LC incidence strongly dependent on the geographic region, therefore, in developed countries is higher than the undeveloped and is raising in Asian countries (2). LC morbidity and mortality is more prevalent among men (1).



In Iran, LC is one of the most common cancers with increasing trend, great economic burden and various pattern in different geographical areas (3). Several risk factors associated with LC may had synergistic effects; smoking, diet, occupational and environmental risk factors, family history and gender, but smoking is the most important risk factor (4).

Therefore, investigating the causes of increased incidence and mortality of LC and associated risk factors is essential for comprehensive health planning for reducing the burden of disease. Since there is no comprehensive study addressing all the epidemiological aspects of this cancer in Iran, therefore, the present study aimed to investigate the epidemiological aspects of LC in Iran.

Methods

This systematic review was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) protocol (5).

Search strategy

The search was performed until the Aug. 2020 on the in international databases (PubMed, web of science, Scopus, Google Scholar, Science Direct, Springer and ProQuest) and national databases (SID: Scientific Information Database, Magiran,

IranDoc, IranMedex and MedLib) without time limitation. Search was performed by Pulmonary Neoplasms, Lung Neoplasm, Neoplasm, Lung, Lung Cancer, Cancer, Pulmonary Cancer, Cancer, Pulmonary, Cancers, Cancer of the Lung, Iran, incidence, death, risk factors keywords and different combinations of them with AND, OR operators.

Inclusion and exclusion criteria

Articles, which revealed different epidemiological aspects including, incidence, mortality, prevalence and risk factors of LC in Iran were included. Studies that did not have access to the full text, editorial letters, case reports and review articles were excluded.

Articles selection

After an initial search and examination of the articles title and abstract, articles full text that were in line with the study, entered in the reading phase and finally the studies matched with the aims of the study were analyzed.

Data Extraction

A table including related variables, sample size, risk factors and severity of relationship was designed (Table 1).

Table 1: Risk factors associated with lung cancer in Iran

<i>Author</i>	<i>publication Year</i>	<i>Location</i>	<i>Sample size</i>	<i>Related factor</i>	<i>Risk index</i>
Nadji SA. (58)	2007	Mazandaran	Case:141 control: 92	active smoking, HPV infection	NA
Hosseini-Khalili A. (53)	2009	Tehran	20 male	mustard gas	NA
Hosseini M. (45)	2009	Tehran	Case:242 Control: 242	Smoking Occupational exposures to inorganic dusts chemical compounds heavy metals	OR(CI): 5.4(3.2-8.9) OR(CI): 4.2(2.8-6.7) OR(CI): 3.4 (2.1-5.6) OR(CI): 3.0(1.3-7.0)
Razmkhah m. (59)	2005	Shiraz	Case: 72 Control: 262	AG genotypes of SDF-1	p-value =0.008

Mosavi-Jarr Ahi A (60)	2009	Iran	12,488,020 men, 677,469 women	occupational exposure	RR(CI):1.9 (1.7–2.1) for high exposure 1.3 (1.2–1.4)for low exposure
Karimzadeh L. (61)	2011	Tehran	Case: 40 Control: 40	consumption of baked bread in traditional oven	OR(CI): 22.6(1.9-270)
Mahaki B. (62)	2011	Iran	-	Smoking	Posterior Median : 1.067
Karimzadeh L. (56)	2012	Tehran	Case: 50 Control: 50	nitrate and nitrite	OR(CI): 2.7(0.13-0.96)
Masjedi MR. (49)	2013	Tehran	case: 242 Control: 484	Smoking Male/ Female	OR(CI): 6.2 (3.3–11.6) OR(CI): 3.1 (1.2-8.1)
Hosseini M. (47)	2014	Tehran	case: 242 Control: 484	Bread Rice beef (Upper third month) But-ter Middle third month Upper third month Whit e chees e Upper third month Yo-gurt Middle third month Upper third month vegetable ghee animal ghee	OR(CI): 1.54 (1.02-2.32) OR(CI): 1.84(1.17-2.89) OR(CI): 2.67 (1.39-5.10) OR(CI): 1.70(1.07-2.71) OR(CI): 2.94 (1.79-4.82) OR(CI): 3.87 (2.52-2.93) OR(CI): 6.52 (3.49-12.18) OR(CI): 2.37 (1.46-3.83) OR(CI): 2.98 (1.77-5.00) OR(CI): 2.27 (1.17-4.40) OR(CI): 7.71 (3.17-18.74)
Najafi F. (48)	2016	Iran	413591	-daily cigarette smoking -low consumption of vegetables	NA NA
Safari A. (63)	2016	Tehran	490	Opium consumption	NA
Dehghani M. (64)	2018	Yasuj	Case:34 Control: 61	C allele rs2645429 in Farnesyl-Diphosphate Farnesyltransferase 1	OR(CI): C allele 2.71(1.12-6.59) CC : 3.02(1.09-8.39)
Motovali-Bashi M. (65)	2012	Isfahan	Case: 65 Control: 80	possessed heterozygous (*1/*2A) genotype	OR(CI): 2.79(1.01-7.65).
Zafarghandi MR. (51)	2013	Iranian veterans	7,570exposed and 7,595 unexposed with 25-year	Sulfur mustard exposure	Incidence rate ratio: 1.81 (95 % CI 1.27–2.56), Age adjusted incidence rate ratio 1.64 (95 % CI 1.15–2.34),

			follow-up	HR of cancer: 2.02 (95 % CI 1.41–2.88).
Keeley (66)	BR.	2014	Golestan Case: 78 Control: 81	G-CSF GM-CSF OR: 27.7 OR: 13.3
Nikseresht (67)	M.	2018	Yasuj Case: 34 Control: 50	C-allele of the rs2245214 ATG5 gene polymorphism OR(CI): 3.52(1.33-9.26)
Adibhesami (68)	G.	2018	Tehran Case: 120 Control: 120	T0M1 / T1M1 genotype was OR(CI): 3.46(1.61-7.46)
Rahmati (69)	A.	2016	Golestan 50,045 adults enrolled from 2004 to 2008, followed annually until June 2015	Opium use HRs (1.73 (95% CI: 0.99–3.03))
Eydian Z. (70)		2016	Zabol Case: 200 Control: 200	P53 codon 72 polymorphism Non-significant
Motovali-Bashi M. (71)		2014	Isfahan Case: 288 Control: 352	<i>Lys751Gln</i> polymorphism <i>751Gln/Gln</i> genotype OR(CI):1.8(I 0.848-3.819) OR(CI): 0.7(0.307-1.595).
Karimzadeh L. (56)	L.	2012	Tehran Case: 40 Control: 40	Animal sources of nitrate and nitrite intake fruit intake OR(CI): 2.7(0.13-0.9) OR(CI): 0.26 (1.3-11)
Rikhtegar (72)	S.	2018	Tehran Case: 50 Control: 50	KRAS NRAS expression levels P-value :0.01 P-value :0.001
Ahmadi (73)	M.	2018	Yazd Case: 96 Control: 100	CHRNA3 rs1051730 single nucleotide polymorphism Non-significant
Chitsaz (74)	M.	2018	Tehran Case: 50 Control: 50	Expression of EGFR And FGFR4 Genes P-value :0.003
Amini F. (75)		2017	Isfahan Case: 61 Control: 111	miR-214-binding site polymorphism in EGFR Non-significant
Motovali-Bashi M. (76)		2012	Isfahan Case: 120 Control: 100	Distribution of C(-1562)T genotype in type IV collagenase promoter OR(CI): 19.89 (3.21-120.60) in age group of < 60 yr
Motovali-Bashi M. (35)		2012	Isfahan Case: 172 Control: 123	gelatinase B genotype OR(CI): 2.56(0.06-23.82)
Motovali-Bashi M. (77)		2012	Isfahan Case: 112 Control:	T/C single nucleotide polymor- P-value :0.001

			120	phism in CYP1A1 gene	
				C allele	P-value : 0.0001
Motovali-Bashi M. (78)	2013	Isfahan	Case: 120 Control: 110	-765G/C polymorphism of cyclooxygenase 2 genes	P-value : 0.06
Rashidi M. (55)	2014	Isfahan	-	Arsenic	-
Mobasheri MR. (58)	2014	-	-	particulate matter <2.5 micrometers	R=0.65
Ghayyoumi M. (79)	2015	Shiraz	Case: 50 Control: 38	Serum level of Triose Phosphate Isomerase	P-value: 0.76
Hamed F. (80)	2017	Fars	Case: 100 Control: 100	Gln/Gln in male.	P-value: 0,044
Keshvary Rav-an H. (81)	2017	<i>Shabrekor d</i>	Case: 50 Control: 77	All c Alle t	In: Case 90%, control 82% In: Case 10% control 16.2%
Sazgar H. (82)	2017	<i>Shabrekor d</i>	Case: 100 Control: 100	CT genotype	OR(CI): 3.59(2.04-6.69)

Results

Description of studies

Details are listed in Figure 1.

Incidence

LC in Iran was in low rate in 2002, so it was not among the five most common cancers in Iran, although its important mortality rate (6), but the incidence of lung cancer is rising in all parts of Iran (7-9) with an estimation of 5829 cases in 2010 (10).

According to the studies, LC has different rank as a most common cancer in various part of Iran, so that, in 2003, in northwest of Iran was the third most common cancer in men (ASR= 7.9) and the fifth most common cancer in women (ASR= 3.6) (11), the second place among men in Kerman in 2007 (ASR= 7.1) (12), the fourth place in men from 2004 to 2006 in Ardabil province (13), the third place in Golestan Province and in Khuzestan Province (15.4%) (14), the third place

in men and the fifth place in women (15), the third place among men in Kerman (ASR= 14.6) (16) and the fifth place in east Azerbaijan (ASR=15.4) (17). In Birjand it reported as one of the ten most common cancers (18). In Tehran, the incidence of LC was 10.4% in men and 5% in women (19) and in another one, as the third most common cancer in men (ASR= 14.9) and women (ASR=7) (20). Lung and bronchus are the third most common cancers in women (2.9 per 100,000) and men (6.3 per 100,000) (21). In addition, it is the fourth most common cancer in both gender (22). In Tehran, LC was one of the ten most common cancers in both gender for elders (23).

Incidence of LC among men in Kerman is 5.85, 4.47, 3.93, 5.35, 7.92, 10.11 in 2004, 2005, 2006, 2007, 2008, 2009 respectively (24). In Kermanshah Province, LC accounts for 17.6% of men's cancer and 7.3% of women's (25). In north of Iran, 14% of diagnosed cancers are LC (26).

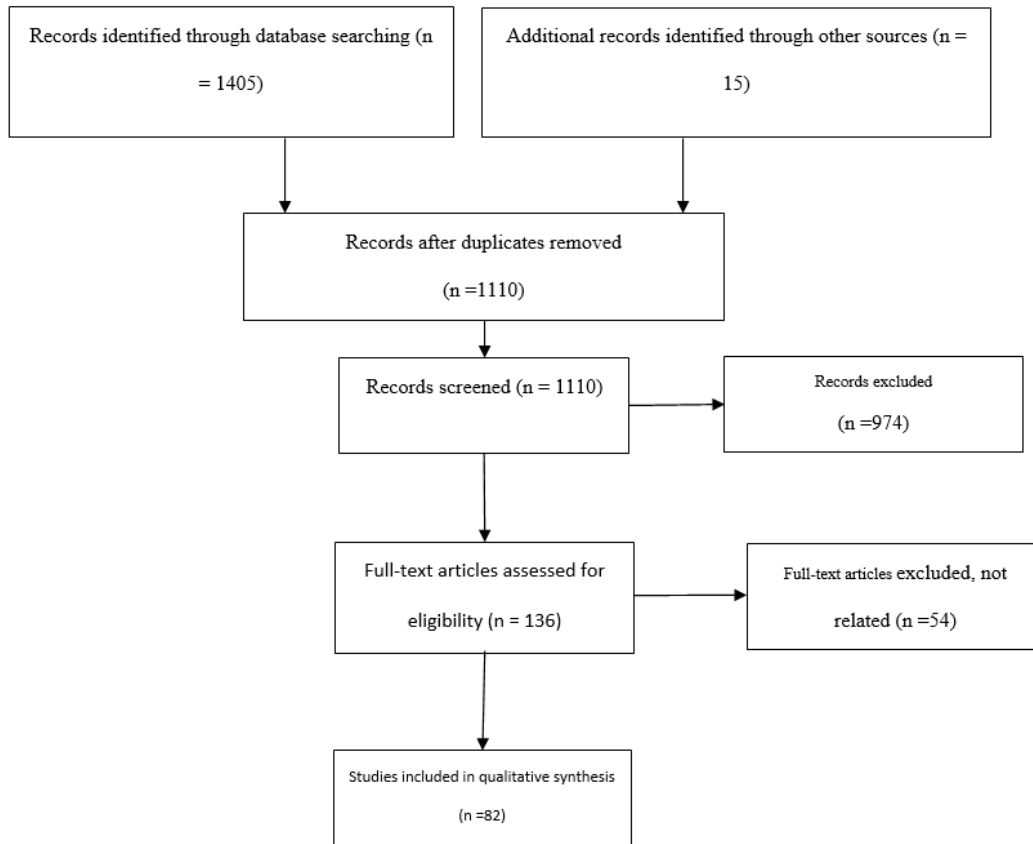


Fig. 1: Flow chart of included study

Prevalence and mortality

The 5-year prevalence of LC in Iran has been reported as 4.21 per 100,000 population, and with a male to female sex ratio of 2.01 (27), in Isfahan, period prevalence of Lung and bronchial cancer were estimated as 9.7% (28).

Based on Global Burden of Disease LC is ranked 28th among the causes of DALYs in Iran (29). Therefore, 120,022 deaths occurred due to LC from 1990 to 2015 in the entire population (36,729 deaths in females and 83 293 in males) (30), with the highest percentage among the 60–79-aged individuals (31).

According to the estimations in 2012, 4,361 deaths from LC and 4,888 new cases were registered in Iran, more incidence and deaths have been reported for men (7). Overall, 9,071 number of deaths from LC occurred in Iran in 2020 and

accounted as the second leading cause of cancer death in Iran (32).

Gender and Age

In Iran, the incidence of the LC is higher in men than women (25); approximately 3 times higher and the highest incidence is in the age group of 80–84 (33, 34).

In Shiraz, 74.2% (35); Ardabil more than 80% (36); Sari, 74.2% and western Iran 83% of LC patients were men (37). For the age group over 65, lung and bronchial cancer are the fifth most common cancer in male (69.54) (15). The mean age of patients reported in a study 58.96 yr (38) in Isfahan, 65.8 yr (28), in chaharmahal Bakhtiari, 60.89 yr (39) and in western of Iran, 61.11 yr (37). In Ardabil in 2011 to 2016, mean age of patients was 65.51 ± 13.8 (40). In Isfahan 94% of LC occurred between the 40 to 90 ages (28).

In Iran the highest incidence was in the sixth decade of life and in men (7) and in Sari was more observed among older patients (25%) (37).

Histology

The squamous cell carcinoma (SCC) and adenocarcinoma (AC) are the most common type of LC in men and women in Iran, respectively (27, 34) and 85.3% of the patients had advanced stages of disease (38). In south of Iran, SCC is the most common type of LC (17). SCC, AC, and small cell carcinoma (SC) were the most common types of LC in Qazvin, respectively (41). In west of Iran, SCC was reported as the most common malignancy (37) from (22.5%) (42) to (61.3%) (36) in different studies and AC (23.5%) (42). In south of Iran, 78.6% of patients were non-small cell and most patients were diagnosed with advanced or metastatic disease (43).

Cost

The estimated cost of LC in Iran in 2014 was reported 3,225,998,555,090 Iranian Rial and its annual cost is estimated as 76,617,943 US \$ (3). In other investigation, the average cost of treating LC for one visit was reported 183 US Dollar for patients (44).

Risk factors

Cigarettes

Smoking is reported as the main cause of LC in Iran (36, 45, 46) and Odds Ratio of LC in smokers were reported 5.4 (95% CI: 3.2-8.9) (47) with a significant relationship with LC in smoker women (48). Smoking and opioid use simultaneously, are a serious risk factors for LC progression (49). Smoking increases the cost of LC, and men have higher risk than women (46). In another research, in current and former smokers, hospitalization and hospital costs increased in LC patients by 48 and 35%, respectively, compared to patients who never smoked (50).

Opium use

Opium use, with a relative risk adjusted for other variables in the cohort study in north of Iran for those who had consumed opium, at 1.73 for LC.

The risk elevates with increasing duration of use, so that, the relative risk of opioid consuming less than 10 yr reported a relative risk of 2.42 (51).

HPV infection

HPV infection has been implicated as a risk factor in LC progression (52).

Mustard gas

Findings show that the LC in persons who have exposed to mustard gas started in lower ages (53) and the mean age among them is decreased to 48 ± 12 (6).

Occupational exposure

Recent studies have reported strong associations between LC and occupation and the environment in Iran with a chance of 4.2, (95% CI 2.8-6.7) (45). Reported associated workplace exposure are smoke and steam and number of metals, including arsenic, chromium, and nickel (54). Significantly increased risk of LC was observed in patients who exposed with inorganic dusts, heavy metals 3.0 (95% CI 1.3-7.0) and chemical compounds 3.4 (95% CI 2.1-5.6) (45). Arsenic in fertilizers has been reported as LC risk factor (55).

Nitrites

Positive relationship between animal sources of nitrite and LC has observed (OR = 2.7 95% CI: 0.13-0.96) (56).

Diet

Bread, rice, beef, liver, dairy products, animal and vegetable oils are known as risk factors for lung cancer in Iran (47). Fruit consumption significantly reduces LC risk (OR=0.26) (56), whereas low vegetable consumption regarded as a risk factor for LC (48).

Environmental factors

According to a study in Tehran, air pollution, dust and the presence of pollutants in the environment are associated with an increased risk of LC mortality (57) and suspended particles below 2.5 micron has been identified as a risk factor for LC with a coefficient of 0.43 (58).

Genetic Factors

Genetic polymorphisms and genetic defects can increase the risk of LC, details of factors associated with LC are presented in Table 1.

Discussion

This systematic review investigated the epidemiological aspects of LC in Iran. In general, LC is one of the most common cancers in Iran and has high mortality. Its incidence is rising in all parts of Iran (8, 9, 33) with an estimation of 5829 cases in 2010 (10). Moreover, the number of LC deaths increased from 4,361 in 2012 (7) to 6,124 in 2018, so LC is the second leading cause of cancer death in Iran, with accounting 11% of cancer deaths (32).

Some of the most significant risk factors for LC incidence are smoking, unhealthy diet, alcoholic drinks, the chemical quality of drinking water, vegetables, fruits and micro-nutrients, occupational exposures, air pollution, benign lung disease such as asthma and tuberculosis, gender and race (4). In Iran, the main cause of LC is smoking (45, 46) and due to smoking, men have higher risk than women (46).

While increasing trend of LC incidence and mortality in Asian and African countries (83); in Denmark, UK and USA the mortality rate has been decreased due to implementation preventive programs for decreasing the smoking habit and lifestyle changing (84). Asian countries observed a sharp increase in the incidence and mortality rate of LC, due to increasing smoking trend in recent decades (85).

Initiation of preventive programs in recent years may lead to lower smoking in one or two decade, and if would be implemented appropriately, can reduce the increasing trend of LC in less than two decades (86). Thus, decreased smoking or quitting it, as a most effective approach, must be the focus of the public, policy makers, and planners worldwide (87).

Consumption vegetables and fruits is recommended as one of the key strategies in lowering down LC cases and increased consumption of

high fat and fried food are considered as a risk factor and according to the prevalence of this risk factor in contemporary society, it became more significant than in the past and needs to proper planning (4, 48).

Mustard gas is one of the causes of LC that many people were exposed to it during the Iran-Iraq war (51). Some studies have reported strong associations between LC and occupation and the environment in Iran (36) such as exposure to smoke and steam and number of metals, including arsenic, chromium, and nickel (59). Therefore, it's necessary to plan effectively for reducing the exposure time and increasing the safety equipment usage by workers and employers (45, 54, 55).

Environmental pollutions are considered as possible risk factors of LC. Thus, policy making for controlling and reduction of them, seems to be necessary to future control of LC (55, 58).

Conclusion

The incidence and mortality of LC in Iran is rising, while many of its risk factors can be modified; so planning to inform and reduce the risk factors is suggested. Smoking is the most important risk factor for LC, so reducing smoking is the most efficient action.

Ethical considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflicts of interest

There are no conflicts of interest.

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