



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 Whitcheese Middle third month 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)		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	P-value : 0.0001
Motovali-Bashi M. (78)	2013	Isfahan	Case: 120 Control: 110	C allele -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).

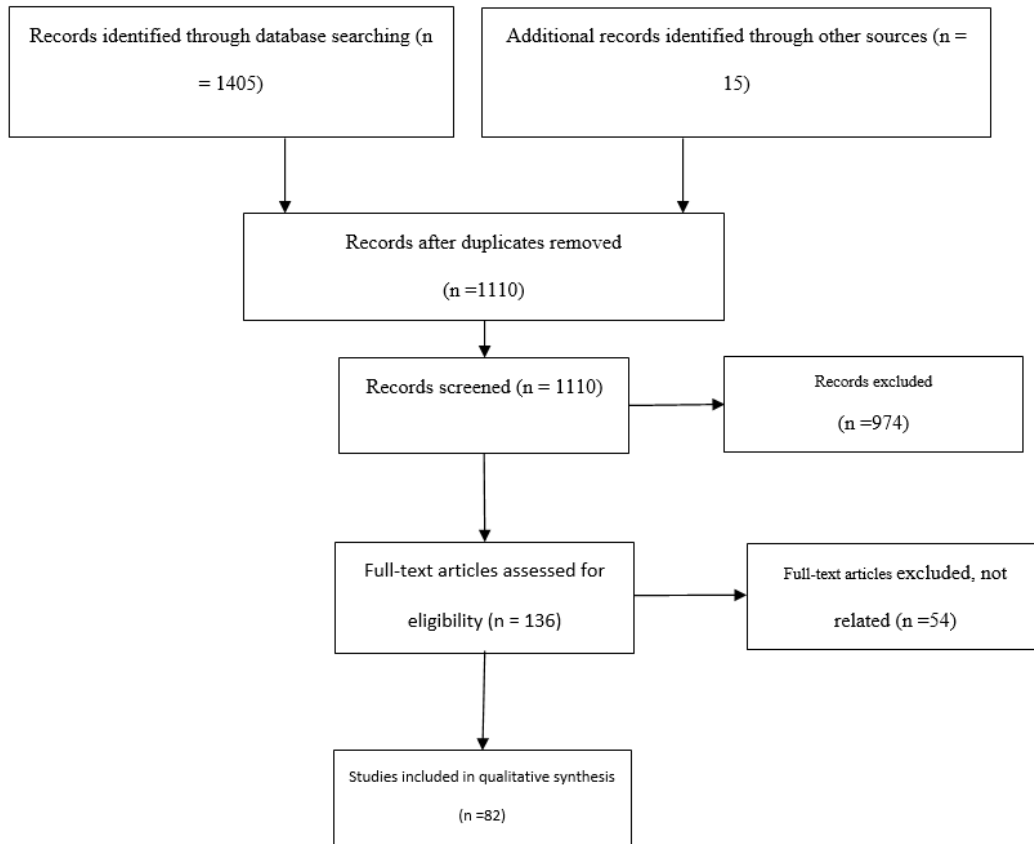


Fig. 1: Flow chart of included study

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.

References

1. Siegel RL, Miller KD, Jemal A (2019). Cancer statistics. *CA Cancer J Clin*, 69(1): 7-34.
2. Wong MCS, Lao XQ, Ho K-F, et al (2017). Incidence and mortality of lung cancer: global trends and association with socioeconomic status. *Sci Rep*, 7(1): 14300.
3. Roshandel G, Ghanbari-Motlagh A, Partovipour E, et al (2019). Cancer incidence in Iran in 2014: Results of the Iranian National Population-based Cancer Registry. *Cancer Epidemiol*, 61: 50-8.
4. Sadeghi-Gandomani H, Asgari-Tarazoj A, Ghoncheh M, et al (2017). Lung cancer in the world: the incidence, mortality rate and risk factors. *WCRJ*, 4: e911.
5. Moher D, Liberati A, Tetzlaff J, et al (2009). Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ*, 339: b2535.
6. Sadjadi A, Nouraiie M, Mohagheghi MA, et al (2005). Cancer occurrence in Iran in 2002, an international perspective. *Asian Pac J Cancer Prev*, 6(3): 359-63.
7. Almasi Z, Mohammadian-Hafshejani A, Salehiniya H (2016). Incidence, mortality, and epidemiological aspects of cancers in Iran; differences with the world data. *J BUON*, 21(4):994-1004.
8. Bab S, Abdifard E, Moradi Y, et al (2016). Lung cancer incidence trends in Iran and in six geographical regions of the country (2000 - 2005). *Shiraz E Medical Journal*, 17(6): e38237.
9. Enayatrad M, Mirzaei M, Salehiniya H, et al (2016). Trends in Incidence of Common Cancers in Iran. *Asian Pac J Cancer Prev*, 17(S3):39-42.
10. Mohagheghi MA, Mousavi-Jarrahi Y, Mosavi-Jarrahi A (2011). Cost of care for lung cancer in the first year after diagnosis in Iran. *Asian Pac J Cancer Prev*, 12(4):1013-5.
11. Sadjadi A, Malekzadeh R, Derakhshan M, et al (2003). Cancer occurrence in Ardabil: Results of a population-based Cancer Registry from Iran. *Int J Cancer*, 107: 113-8.
12. Sajadi A, Zahedi MJ, Moghadam SD, et al (2007). The First Population-Based Cancer Survey in Kerman Province of Iran. *Iran J Public Health*, 36(4): 26-34.
13. Babaei M, Jaafarzadeh H, Sadjadi AR, et al (2009). Cancer Incidence and Mortality in Ardabil: Report of an Ongoing Population-Based Cancer Registry in Iran, 2004-2006. *Iran J Public Health*, 38(4): 25-35.
14. Roshandel G, Sadjadi A, Aarabi M, et al (2012). Cancer incidence in golestan province: report of an ongoing population-based cancer registry in Iran between 2004 and 2008. *Arch Iran Med*, 15(4): 196-200.
15. Amoori N, Mirzaei M, Cheraghi M (2014). Incidence of Cancers in Kuzestan Province of Iran: Trend from 2004 to 2008. *Asian Pac J Cancer Prev*, 15(19): 8345-9.
16. Shahesmaeili A, Afshar R.M, Sadeghi A, et al (2018). Cancer incidence in Kerman Province, Southeast of Iran: Report of an ongoing population-based cancer registry, 2014. *Asian Pac J Cancer Prev*, 19(6): 1533-41.
17. Somi Mh, Mousavi Sm, Rezaeifar P, et al (2009). Cancer incidence among the elderly population in the northwest of Iran: a population based study. *Int J Cancer*, 2(3): 117-26.
18. Mezginejad F, Haghghi F, Behravan M, et al (2016). Cancer Types in Pathological Samples Referred to Educational Hospitals in Birjand During the Past Three Years (2011 - 2013). *Int J Cancer Manag*, 9(5): e4075.
19. Kolahi AA, Mosavi-Jarrahi A (2007). Incidence of occupational lung cancer in Tehran-Iran. *Journal of Thoracic Oncology*, 2(8):S343-S4.
20. Mohagheghi Sma, Mousavi Jarahi Sar, Malekzadeh R, et al (2009). Cancer incidence in Tehran metropolis: the first report from the tehran population-based cancer registry, 1998 – 2001. *Arch Iran Med*, 12(1): 15-23.
21. Masoompour SM, Yarmohammadi H, Rezaianzadeh A, et al (2011). Cancer incidence in southern Iran, 1998–2002: Results of population-based cancer registry. *Cancer Epidemiol*, 35(5):e42-7.
22. Karami K, Cheraghi M, Amori N, et al (2014). Common Cancers in Khuzestan Province, South West of Iran, during 2005-2011. *Asian Pac J Cancer Prev*, 15(21):9475-8.
23. Rohani-Rasaf M, Rohani-Rasaf MR, Hashemi Nazari SS, et al (2017). Cancer Incidence Rate in the Elderly Inhabitants of Tehran: Is there really any Cluster? *Int J Cancer Manag*, 10(7):e5753.

24. Keyghobadi N, Rafiemanesh H, Mohammadian-Hafshejani A, et al (2015). Epidemiology and trend of cancers in the province of Kerman: southeast of Iran. *Asian Pac J Cancer Prev*, 16(4): 1409-13.
25. Rahimi Z, Kasraei R, Najafi F, et al (2015). Cancer notification at a referral hospital of Kermanshah, Western Iran (2006-2009). *Asian Pac J Cancer Prev*, 16(1): 133-7.
26. Bozorgi F, Hedayatizadeh-Omran A, Alizadeh-Navaei R, et al (2017). Causes of Death of Cancer Patients in a Referral Hospital in Northern Iran between 2013 and 2016. *WCRJ*, 4 (3): e909.
27. Vardanjani HM, Zeinali M, Radmerikhi S, et al (2017). Lung Cancer Prevalence in Iran by Histologic Subtypes. *Adv Biomed Res*, 6:111.
28. Tolou Ghamari Z (2018). Prevalence of lung cancer in Isfahan Province, Iran. 2018. *J Egypt Natl Canc Inst*, 30(2): 57-9.
29. Modirian M, Rahimzadeh S, Cheraghi Z, et al (2015). Burden of Cancers in Iran from 1990 to 2010: findings from the Global Burden of Disease study 2010. *Arch Iran Med*, 18(10): 629-37.
30. Rajai N, Ghanbari A, Yoosefi M, et al (2020). National and subnational trends in incidence and mortality of lung cancer in Iran from 1990 to 2016. *Asia Pac J Clin Oncol*, 16(3): 129-36.
31. Ghasemi S, Mahaki B, Dreassi E, et al (2020). Spatial Variation in Lung Cancer Mortality and Related Men-Women Disparities in Iran from 2011 to 2014. *Cancer Manag Res*, 12: 4615-24.
32. Global Cancer Observatory (2021). Iran-islamic-republic-of-fact-sheets: The Global Cancer Observatory. International Agency for Research on Cancer, Lyon, France. Available from: <https://gco.iarc.fr/today/data/factsheets/populations/364-iran-islamic-republic-of-fact-sheets.pdf>.
33. Almasi Z, Salehiniya H, Amoori N, et al (2016). Epidemiology Characteristics and Trends of Lung Cancer Incidence in Iran. *Asian Pac J Cancer Prev*, 17(2): 557-62.
34. Khazaei S, Mansori K, Soheylizad M, et al (2017). Epidemiology of lung cancer in Iran: Sex difference and geographical distribution. *Middle East Journal of Cancer*, 8: 223-8.
35. Motovali-bashi M, Taghvaei S, Hemati S (2012). The Association between Gelatinase B and Lung Cancer in Smokers and Non-Smokers. *Journal of Isfahan Medical School*, 30:1393-402.
36. Ghobadi H, Sharghi A, Sadat-Kermani J (2013). Epidemiology and Risk Factors for Lung Cancer in Ardabil, Iran. *JArUMS*, 13(2): 220-8.
37. Abbasi M, Moradi F, Esna-Ashari F, et al (2019). Epidemiological and Pathological Study of Lung Cancer in Patients Referred to Ekbatan and Shahid Beheshti Hospitals in Hamadan during 2001 - 2016. *Avicenna Journal of Clinical Medicine*, 25(4): 236-43.
38. Adnan K, Esfahani-Monfared Z, Sei S, et al (2016). Clinicopathological Characteristics of Iranian Patients with Lung Cancer: a Single Institute Experience. *Asian Pac J Cancer Prev*, 17(8): 3817-22.
39. Shahbazi-Gahrouei D, Danesh A (2004). Investigation of cancers incidence relevant to radiation in Chaharmahal and Bakhtiari province during five years (1998-2002). *J Shahrekord Univ Med Sci*, 6(1):7-13.
40. Adham D, Asl E, Abbasgholizadeh N, et al (2019). Spatial Analysis and Epidemiology of Lung Cancer in the Northwest of Iran. *PJM H S*, (12): 20181851.
41. Hajmanoochehri F, Mohammadi N, Zohal MA, et al (2014). Epidemiological and clinicopathological characteristics of lung cancer in a teaching hospital in Iran. *Asian Pac J Cancer Prev*, 15(6):2495-500.
42. Salari A, Taghipour S, Moghimi M, et al (2012). Evaluation of frequency of clinical and pathological findings in lung diseases in shahid Sadoughi University of medical sciences of yazd, during 2001-2006. *Iranian Journal of Surgery*, 20(1): 27-33.
43. Abedi S, Janbabaee G, Moosazadeh M, et al (2017). Epidemiology of Lung Cancer Patients Attending Tooba Clinic and Imam Khomeini Hospital, Sari, Iran 2010-2014. *J Mazandaran Univ Med Sci*, 27(151): 86-93.
44. Akbarzadeh Ba, Esmaeili M, Kimiafar K (2009). Medical information management and assessment of direct costs of treatment of lung cancer. *Health Information Management*, 5(2):151-8.
45. Hosseini M, Naghan PA, Karimi S, et al (2009). Environmental risk factors for lung cancer in

- Iran: a case-control study. *Int J Epidemiol*, 38(4): 989-96.
46. Ghobadi M, Farrokhi MR, Nakhaee N, et al (2017). Estimation of the Cost of Smoking-Attributable Diseases (Five Selected Diseases): A Case in Kerman City, Iran, 2014. *Addict Health*, 9(4): 190-8.
 47. Hosseini M, Naghan PA, Jafari AM, et al (2014). Nutrition and lung cancer: a case control study in Iran. *BMC Cancer*, 14: 860.
 48. Najafi F, Moradinazar M, Barati M JT, et al (2016). Correlation between risk factors for non-communicable diseases and common cancers in Iran: Ecological study. *International Business Management*, 10(15):3015-9.
 49. Masjedi MR, Naghan PA, Taslimi S, et al (2013). Opium Could Be Considered an Independent Risk Factor for Lung Cancer: A Case-Control Study. *Respiration*, 85(2):112-8.
 50. Akbari AB, Rezaei S, Arab M, et al (2016). Effects of Smoking on Cost of Hospitalization and Length of Stay among Patients with Lung Cancer in Iran: a Hospital-Based Study. *Asian Pac J Cancer Prev*, 17(9):4421-6.
 51. Zafarghandi MR, Soroush MR, Mahmoodi M, et al (2013). Incidence of cancer in Iranian sulfur mustard exposed veterans: a long-term follow-up cohort study. *Cancer Causes Control*, 24(1): 99-105.
 52. Nadji SA, Mahmoodi M, Ziaee AA, et al (2007). An increased lung cancer risk associated with codon 72 polymorphism in the TP53 gene and human papillomavirus infection in Mazandaran province, Iran. *Lung Cancer*, 56(2): 145-51.
 53. Hosseini-khalili A, Haines DD, Modirian E, et al (2009). Mustard gas exposure and carcinogenesis of lung. *Mutat Res*, 678(1): 1-6.
 54. Alberg AJ, Yung RC, Strickland PT, J. N (2002). Respiratory cancer and exposure to arsenic, chromium, nickel, and polycyclic aromatic hydrocarbons. Clinics in Occupational and Environmental Medicine. *Bloomberg School of Public Health*, 2(4): 779-801.
 55. Rashidi M, Rameshat MH, R. R (2014). Geographic Health and Human Health; Using Space Technology and Remote Sensing in Monitoring Soil Pollution by Arsenic and the Related Lung Cancer in Isfahan, Iran: A Case Study. *Journal of Isfahan Medical Sciences*, 32(287): 784-90.
 56. Karimzadeh L, Koohdani F, Siassi F, et al (2012). Relation between nitrate and nitrite food habits with lung cancer. *J Exp Ther Oncol*, 10(2):107-12.
 57. Hadei M, Hashemi Nazari SS, Yarahmadi M, et al (2017). Estimation of Gender-Specific Lung Cancer Deaths due to Exposure to PM2.5 in 10 Cities of Iran during 2013 - 2016: A Modeling Approach. *Int J Cancer Manag*, 10(8):e10235.
 58. Mobasheri MR, A. H (2014). Using Satellite Images for Determination of Critical Points in Polluted Cities and their Relation to Lung Cancer Affection. *Hakim Health Systems Research Journal*, 17(2):151-8.
 59. Razmkhah M, Doroudchi M, Ghayumi SM, et al (2005). Stromal cell-derived factor-1 (SDF-1) gene and susceptibility of Iranian patients with lung cancer. *Lung Cancer*, 49(3):311-5.
 60. Mosavi-Jarrahi A, Mohagheghi M, Kalaghchi B, et al (2009). Estimating the incidence of lung cancer attributable to occupational exposure in Iran. *Popul Health Metr*, 7:7.
 61. Karimzadeh L, Koohdani F, Siassi F, et al (2011). A case control study on the lung cancer risk factors in north of Iran. *J Exp Ther Oncol*, 9(2): 153-8.
 62. Mahaki B, Mehrabi Y, Kavousi A, et al (2011). Multivariate disease mapping of seven prevalent cancers in Iran using a shared component model. *Asian Pac J Cancer Prev*, 12(9): 2353-8.
 63. Safari A, Reazai M, Tangestaninejad A, et al (2016). Opium consumption: A potential risk factor for lung cancer and pulmonary tuberculosis. *Indian J Cancer*, 53(4): 587-9.
 64. Dehghani M, Samani Z, Abidi H, et al (2018). Relationship of SNP rs2645429 in Farnesyl-Diphosphate Farnesyltransferase 1 Gene Promoter with Susceptibility to Lung Cancer. *Int J Genomics*, 2018:4863757.
 65. Motovali-Bashi M, Biglari M, Hojati Z, et al (2012). Role of CYP1A1 MspI polymorphism in CYP1A1 gene with susceptibility to lung cancer in Iranian patients. *J Res Med Sci*, 17(5):1.
 66. Keeley BR, Islami F, Pourshams A, et al (2014). Prediagnostic serum levels of inflammatory biomarkers are correlated with future development of lung and esophageal cancer. *Cancer Sci*, 105(9):1205-11.

67. Nikseresht M, Shahverdi M, Dehghani M, et al (2018). Association of single nucleotide autophagy-related protein 5 gene polymorphism rs2245214 with susceptibility to non-small cell lung cancer. *J Cell Biochem*, 120(2):1924-31.
68. Adibhesami G, Shahsavari GR, Amir A, et al (2018). Glutathione S-transferase M1 (GSTM1) and T1 (GSTT1) Polymorphisms and Lung Cancer Risk among a Select Group of Iranian People. *Asian Pac J Cancer Prev*, 19(10): 2921-7.
69. Rahmati A, Shakeri R, Khademi H, et al (2017). Mortality from respiratory diseases associated with opium use: a population-based cohort study. *Thorax*, 72(11): 1028-34.
70. Eyadian Z, Asna'ashari AM, Behravan J, et al (2016). Association of P53 codon 72 polymorphism and lung cancer in an ethnic Iranian population. *Cell Mol Biol (Noisy-le-grand)*, 62(9):34-8.
71. Motovali-Bashi M, Rezaei H, Dehghanian F, et al (2014). Association between XPD (Lys751G1n) Polymorphism and Lung Cancer Risk: A Population-Based Study in Iran. *Cell J*, 16(3): 309-14.
72. Rikhtegar S, Hesampour A (2018). Investigation of KRAS and NRAS expression levels in lung cancer patients compared to normal patients. *Yafte*, 20(3): 19-27.
73. Ahmadi M, Moshtaghioun SM, Falahati A (2018). Association of the CHRNA3 rs1051730 single nucleotide polymorphism with lung cancer risk in Iranian patients. *JSSU*, 26(7): 599-606.
74. Chitsaz M, Hesampour A (2018). Investigating the Expression of EGFR and FGFR4 Genes in Patients with Lung Cancer. *JBUMS*, 20(4): 17-23.
75. Amini F, Motovalli Bashi M, Hemmati S (2018). Study of egfr gene in relationship between polymorphism and mir-214 binding site in lung cancer. *Pejoubesh dar Pezesbki (Research in Medicine)*, 41(4): 268-274.
76. Motovali-bashi M, Taghvaei S, Hemati S (2012). The association between the C(-1562)t polymorphism of type IV collagenase gene and reduced age of onset of lung cancer. *Journal of Isfahan Medical School*, 30(203): 1-9
77. Motovali-Bashi M, Bordbar M, Rezaei H (2012). Study of association between T/C single nucleotide polymorphism in CYP1A1 gene and cancer initiation and smoking status in lung cancer patients. *Pejoubesh dar Pezesbki (Research in Medicine)*, 36(3): 151-6.
78. Motovali-Bashi M, Hojati Z (2013). Investigation of correlation between -765G/C polymorphism of cyclooxygenase 2 genes and lung cancer in Isfahan population. *Pejoubesh dar Pezesbki (Research in Medicine)*, 37(1): 47-54.
79. Ghayyoumi M, Mansouri M (2015). Determination of Serum level of Triose Phosphate Isomerase in lung Cancer Patients. *Armaghane Danesh*, 19(11): 948-54.
80. Hamed F, Tahmaseb M, A G (2016). Prognostic Importance of Polymorphisms in DNA-Repair Gene (XRCC1 Arg399Gln) in Patients with Lung Cancer in Fars Province, Iran. *Journal of Isfahan Medical School*, 34(403): 1244-50.
81. Keshvary Ravan H, Kouhkan F, Sazgar H (2017). Single Nucleotide Polymorphisms of MMP2 Gene Promoter on the Risk of Development and Metastasis of lung Cancer. *Armaghane Danesh*, 22(1): 104-17.
82. Sazgar H (2017). Evaluation of correlation between -1562 C/T in promoter single nucleotide polymorphisms of MMP-9 gene and lung cancer initiation and metastasis risk. *Pars of Jabrom University of Medical Sciences*, 15(2): 9-16.
83. Pakzad R, Mohammadian-Hafshejani A, Ghoncheh M, et al (2015). The incidence and mortality of lung cancer and their relationship to development in Asia. *Transl Lung Cancer Res*, 4(6): 763-74.
84. Jemal A, Center MM, DeSantis C, et al (2010). Global patterns of cancer incidence and mortality rates and trends. *Cancer Epidemiol Biomarkers Prev*, 19(8):1893-907.
85. Bogos K, Kiss Z, Gálffy G, et al (2019). Revising Incidence and Mortality of Lung Cancer in Central Europe: An Epidemiology Review from Hungary. *Front Oncol*, 9:1051.
86. de Groot P, Munden RF (2012). Lung cancer epidemiology, risk factors, and prevention. *Radiol Clin North Am*, 50(5): 863-76.
87. Jazieh AR, AlGhamdi M, AlGhanem S, et al (2018). Saudi lung cancer prevention and screening guidelines. *Ann Thorac Med*, 13(4):198-204.