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Trends in lung cancer incidence in Iraq during the period 2005-2019

Muzahem M. AL-Hashimi, Mohammed Qasim Yahya Alawjar
Department of Statistics and Informatics, College of Computer Science & Mathematics, University of Mosul, Mosul, Iraq

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ABSTRACT

Lung cancer, a prominent global malignancy and a significant contributor to cancer-related deaths, was examined in Iraq from 2005 to 2019 using data from the cancer registry. Age-standardized incidence rates (ASIR), categorized by sex and age at diagnosis, were analyzed to identify trends, utilizing annual percent change (APC) and average annual percent change (AAPC). During the 2005-2019 period, ASIR was 18.339/100,000 for males and 5.861/100,000 for females. Lung cancer ASIR experienced a notable 48.027% increase, starting at 9.426/100,000 in 2005 and reaching 13.953/100,000 in the most recent year. The rates demonstrated significant growth, with AAPC values of +2.857% for both sexes, +2.495% for males, and +4.474% for females. The highest incidences of lung cancer were among the elderly (70+ years) in both sexes, particularly pronounced in females (8.961%) and males (5.601%). In contrast, the lowest rates were found in individuals aged 0 to 49 years, showing negative APC values: -1.359% (males) and -0.843% (females). The study underscores the escalating prevalence of lung cancer in Iraq, particularly impacting older females. Urgent and targeted efforts are necessary to mitigate the rising incidence rates.

Corresponding Author:

Muzahem M. AL-Hashimi
Department of Statistics and Informatics, College of Computer science & Mathematics,
University of Mosul
Mosul, Iraq
Email: muzahim_alhashime@uomosul.edu.iq

1. INTRODUCTION

In 2020, lung cancer ranked as the second most prevalent malignant neoplasm worldwide and stood as the primary cause of cancer-related fatalities [1]. It constituted 11.4% of all new cancer cases and led to 18.0% of cancer-related deaths, accounting for an estimated 22 million new cases and 1.8 million deaths. While being the foremost cause of cancer-related morbidity and mortality among males, lung cancer held the third place in incidence and the second place in mortality among females, trailing behind breast and colorectal cancers [1]. Geographical variation and sex differences considerably influenced lung cancer incidence rates [2]. Regions like Micronesia/Polynesia (51.6/100,000), Eastern Europe (49.0/100,000), Eastern Asia (48.1/100,000), and Southern Europe (43.1/100,000) displayed the highest incidence rates in males. In contrast, the incidence rates in Africa were generally lower, with figures ranging from intermediate to high in the Southern (27.5/100,000) and Northern regions (19.5/100,000) [1]. For females, Northern America (30.1/100,000), Northern Europe (26.8/100,000), Micronesia/Polynesia (22.9/100,000), and Australia/New Zealand (22.7/100,000) recorded the highest incidence rates [1].

Lung cancer is categorized into two main subtypes: small-cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC), with the latter constituting approximately 85% of all diagnosed lung cancer cases. A

significant majority (85%) of lung cancer cases are diagnosed among individuals with a history of tobacco use, either current or former smokers. Tobacco use has been causally linked to NSCLC, posing a substantial risk to over 500 million smokers worldwide in relation to this lethal cancer [3]–[6].

In Iraq, the total count of cancer cases in 2005 reached 15,172. Among males, the foremost malignancy was bronchus and lung cancer (13.08%), with an incidence rate of 7.22/100,000. Among females, bronchus and lung cancer (3.94%) had an incidence rate of 2.27/100,000. By 2019, the total number of new cancer cases had escalated to 35,864. For males, the top ten malignancies included bronchus and lung cancer (12.39%) with an incidence rate of 10.10/100,000. Among females, bronchus and lung cancer (4.09%) had an incidence rate of 4.31/100,000 [7].

The Iraqi Cancer Registry originated in 1974 through a collaborative effort between the Ministry of Health and the Iraqi Cancer Society. Starting in 1975, the registry initiated annual data collection from medical record departments of all hospitals (public and private), radiation and pathology departments, as well as public and commercial laboratories across Iraq. Annually, the Iraqi Cancer Board within the Ministry of Health releases comprehensive statistical data on cancer in Iraq. This data encompasses the top ten malignancies and details the distribution of cancers across various governorates, age groups, and sexes [7]. This study aimed to investigate the patterns of bronchus and lung cancer incidence rates in Iraq from 2005 to 2019, categorized by sex and age.

2. METHOD

Utilizing data extracted from the Iraqi Cancer Registry (ICR) spanning the years 2005 to 2019, the datasets during the study period are publicly available. These datasets have been published annually since 1976 in the Reports and Results of the Iraqi Cancer Registry, which are printed by the World Health Organization (WHO) [7]. We calculated the age-standardized incidence rates (ASIRs) using the world standard population, and age-specific incidence rates (ASRs) were determined for bronchus and lung cancer (coded as C33 and C34). Cases were stratified into four groups based on sex and age at diagnosis (0–49, 50–59, 60–69, and 70+ years). We analyzed trends in the incidence of combined bronchus and lung cancer across both sexes and within different age groups using Poisson regression, a statistical method derived from generalized linear models commonly employed to investigate temporal trends in cancer incidence or chronic diseases. The Joinpoint software, version 4.9.0.0 (National Cancer Institute), was utilized to estimate the annual percentage change (APC) and average annual percentage change (AAPC) of the natural log-transformed rates for each calendar year as a regression variable. This analysis aimed to assess changes in ASRs over time.

The Joinpoint software required the predefined specification of a minimum (0) and maximum (>0) number of joinpoints. For our study, the minimum number of joinpoints was set at zero, while the maximum was set at four. We assumed homoscedastic random errors. Joinpoints were identified using a grid search approach. Model selection employed sequential permutation tests to ascertain the optimal number of joinpoints, with Monte Carlo simulation employing 4,499 permutations for accurate calculation. In all our analyses, a significance level of p-value 0.05 was employed.

3. RESULTS AND DISCUSSION

Between 2005 and 2019, a total of 28,118 cases of lung cancer were identified. The distribution of these cases by sex, age at diagnosis, and the most prevalent histology is outlined in Table 1. Among these cases, males accounted for 72.437%, while females constituted 27.562%. Notably, lung cancer ranked as the predominant malignancy within the 60 to 69 age group, comprising 35.5% of cases, and stood as the second most common cancer in those aged 70 and older. The predominant histological types were Squamous cell carcinoma, not otherwise specified (NOS), at 25.546%, followed by Adenocarcinoma, NOS, at 19.013%.

Table 1. Demographic Data of all cases of lung cancer in Iraq, (2005-2019)

Demographic data		Number	%
Sex	Male	20,368	72.437
	Females	7,750	27.562
Age at diagnosis	<50 years	3,069	10.915
	50-59 years	5,434	19.326
	60-69 years	9,982	35.500
	70 years and over	9,633	34.259
Most frequent histology	Squamous cell carcinoma, NOS	7,183	25.546
	Adenocarcinoma, NOS	5,346	19.013
	Small cell carcinoma, NOS	1,902	6.764
	Non-small cell carcinoma (12.1)	1,798	6.395
	Epithelial tumor	1,135	4.037
	Bronchiolo-alveolar adenocarcinoma	874	3.108

It was observed that males consistently exhibited higher ASRs for lung cancer compared to females. Throughout the study duration, ASR was measured at 18.339/100,000 for males and 5.861/100,000 for females. Significantly, the incidence ASR for lung cancer escalated by 48.027% across both sexes, with an ASR of 9.426/100,000 in 2005 surging to 13.953/100,000 in the latest year. This surge in incidence was evident across all age groups, with the most substantial increase noted in the 70 and older age category (110.132%).

Specifically for males, the ASR for lung cancer exhibited a significant 40.346% increase, rising from 15.429/100,000 in 2005 to 21.654/100,000 in the latest year. This upward trend was consistent across different age groups, with the 70 and older age group experiencing the most significant increase (79.669%). Similarly, the ASR for female lung cancer incidence witnessed an 84.695% increase, climbing from 4.083/100,000 in 2005 to 7.541/100,000 in 2015. The increase in incidence was observed across various age groups, with the 70 and older category displaying the most substantial increase (236.83%).

Over the period from 2005 to 2019, lung cancer rates demonstrated significantly increase, characterized by an AAPC of +2.857% for both sexes. This increase was marked by two distinct inflection points in 2013 and 2016 Figure 1. Specifically in males, incidence rates displayed a significant upward from 2005 to 2019, with an AAPC of +2.495%. This trend was identified through three joinpoints in 2007, 2013, and 2016 Figure 2. Among females, a similarly significant increase in incidence rates was observed over the entire study period (2005 to 2019), with an AAPC of +4.474%, without any joinpoints detected Figure 3.

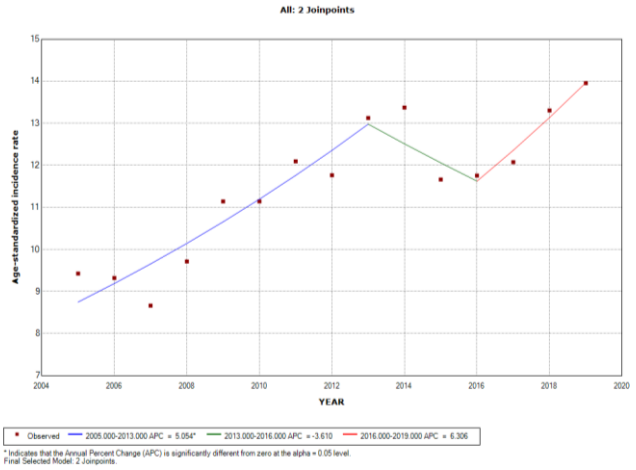

Figure 1. Joinpoint regression of age-standardized incidence of lung cancer (per 100 000) in both sexes in Iraq, all ages, 2005 to 2019

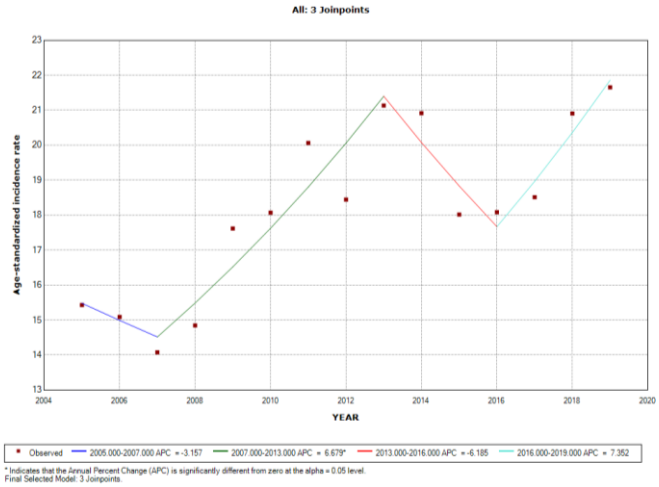

Figure 2. Joinpoint regression of age-standardized incidence of lung cancer (per 100 000) in males in Iraq, all ages, 2005 to 2019

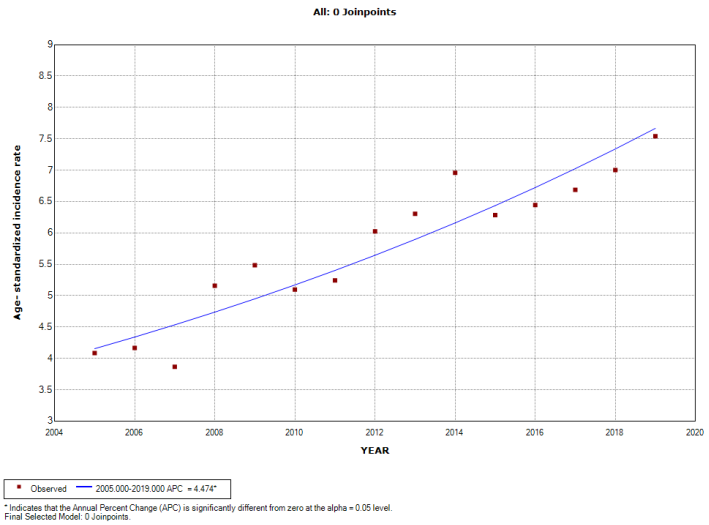

Figure 3. Joinpoint regression of age-standardized incidence of lung cancer (per 100 000) in females in Iraq, all ages, 2005 to 2019

The joinpoint analysis findings for the age group 0-49 indicated that the trend of age-standardized lung cancer incidence rate for both sexes did not exhibit significant decreases from 2005 to 2007, showing an APC of -7.267%. Following this, a non-significant increase was noted from 2007 to 2010, with an APC of +5.932%. This was followed by a significant decrease from 2010 to 2016, characterized by an APC of -5.884%, and a significant increase from 2016 to 2019, marked by an APC of +12.061%. Despite these fluctuations, the overall incidence demonstrated a statistically non-significant decrease over the period 2005 to 2019, with an AAPC of -1.078% (95% CI -2.471, +0.335) Table 2. Males within this age group displayed a statistically significant decrease from 2005 to 2017, with an APC of -2.402%, followed by a non-significant increase from 2017 to 2019, marked by an APC of +13.257%. However, the incidence rates witnessed a statistically significant decrease throughout this period, with an AAPC of -1.359%. Conversely, females in this group did not experience a significant decrease from 2005 to 2019, with an AAPC of -0.843% Table 2.

Table 2. Demographic Data of all cases of lung cancer in Iraq, (2005 to 2019)

Age groups	Sex	Joinpoint location	Trend APC (95% CI)	Trend AAPC (95% CI)
0-49	Both sexes	2005-2007	-7.267 (-19.494, +5.988)	-1.078 (-2.471, +0.335)
		2007-2010	+5.932 (-7.676, +21.546)	
		2010-2016	-5.884* (-8.734, -2.946)	
		2016-2019	+12.061* (+4.616, +20.036)	
	Males	2005-2017	-2.402* (-4.019, -0.758)	-1.359 (-2.743, +0.045)
		2017-2019	+13.257 (-14.515, +50.227)	
50-59	Females	2005-2019	No joinpoint	-0.843 (-2.894, +1.251)
	Both sexes	2005-2019	No joinpoint	-1.019 (-2.370, +0.350)
	Males	2005-2019	No joinpoint	-1.338 (-3.016, +0.368)
	Females	2005-2019	No joinpoint	+0.318 (-0.952, +1.604)
60-69	Both sexes	2005-2010	+9.524* (+4.751, +14.514)	+2.520* (+1.019, +4.043)
		2010-2019	-0.391 (-2.187, +1.437)	
	Males	2005-2010	+9.350* (+4.041, +14.930)	+2.164* (+0.583, +3.770)
		2010-2019	-0.818 (-2.813, 1.218)	
	Females	2005-2014	+7.428* (+5.274, +9.727)	+4.630* (+3.071, +6.212)
		2014-2019	-1.622 (-6.489, +3.498)	
70 and over	Both sexes	2005-2007	-3.456 (-22.382, +20.086)	+6.461* (+5.338, +7.597)
		2007-2013	+9.727* (+4.502, +15.214)	
		2013-2019	+4.096* (+0.327, +8.007)	
	Males	2005-2007	-2.403 (-28.749, +33.685)	+5.601* (+4.227, +6.994)
		2007-2019	+6.244 (+4.285, +8.239)	
	Females	2005-2013	+10.685* (+7.604, 13.853)	+8.961* (+7.756, +10.179)
		2013-2019	+6.425* (+1.872, +11.182)	

For the age group 50-59 in both sexes, the trend remained relatively stable, with no significant decrease observed from 2005 to 2019, as indicated by an AAPC of -1.019%, and no inflection points were identified. In males, the trend displayed a decrease that did not achieve statistical significance from 2005 to

2019, with an AAPC of -1.338%, and no joinpoint were detected. Females within this group, however, exhibited a non-significant increase from 2005 to 2019, showing an AAPC of +0.318, and no joinpoint were observed Table 2.

The trend for both sexes aged 60-69 years increased significantly from 2005 to 2010 with an APC of +9.524%, and then experienced a non-significant decrease from 2010 to 2019 with an APC of -0.391%. However, the incidence increased significantly from 2005 to 2019 with an AAPC of +2.520%. Among males, the trend significantly increased from 2005 to 2010 with an APC of +9.350%, followed by a non-significant decrease from 2010 to 2019 with an APC of -0.818%, while the incidence increased significantly from 2005 to 2019 with an AAPC of +2.164%. Similarly, the trend for females increased significantly from 2005 to 2014 with an APC of +7.478%, followed by a non-significant decrease from 2014 to 2019 with an APC of -1.622%. Nonetheless, the incidence increased significantly over the study period, with an AAPC of +4.630% Table 2.

For the age group of 70 and over for both sexes, the trend decreased not significantly from 2005 to 2007 with an APC of -3.456%, followed by a significant increase from 2007 to 2013 with an APC of +9.727%, and another significant increase from 2013 to 2019 with an APC of +4.096%. Throughout this period, the incidence increased significantly with an AAPC of +6.461%. Among males in this age group, there was a non-statistically significant decrease from 2005 to 2007 with an APC of -2.403%, followed by a significant increase from 2007 to 2019 with an APC of +6.244%. Likewise, the incidence increased significantly over time with an AAPC of +5.601%. Among females in this group, the trend increased significantly from 2005 to 2013 with an APC of +10.685%, and the incidence increased significantly from 2013 to 2019 with an APC of +6.425%. In contrast, males experienced a significant increase in incidence from 2005 to 2019 with an AAPC of +8.961% Table 2.

According to GLOBOCAN 2020, lung cancer stands as the most prevalent cancer globally in terms of both incidence and mortality [1]. Within the Arab world, lung cancer ranks among the top five most common types of cancer, affecting approximately 68.1% of Arab nations [8]. In Iraq, it emerges as the second most frequently occurring cancer, with a notable predominance among males [7].

To the best of our knowledge, this study represents the first attempt to investigate the trajectory of age-standardized lung cancer incidence in Iraq. The main outcome of this analysis, grounded in registry data, reveals a discernible elevation in lung cancer incidence for both males and females across Iraq during the period from 2005 to 2019. For females, the incidence displayed a sustained upward trajectory from 2005 to 2019, while for males, the incidence witnessed two distinctive phases of increase (2007 to 2013 and 2016 to 2019), interspersed with slight decrements in ASIRs during the intervals of 2005 to 2007 and 2013 to 2016. Importantly, the increase persisted as statistically significant for both groups throughout the entire study duration. Our findings indicate that, excluding individuals under the age of 59, females' AAPCs were statistically higher than those of males within the remaining age categories. This aligns with numerous studies conducted in Iraq, suggesting an escalating incidence of lung cancer primarily affecting males, with a tendency to rise with advancing age [9]–[13].

The ASIR for lung cancer in Iraq, among both males and females, was registered as 18.339/100,000 and 5.861/100,000, respectively. These values exhibit comparability to data documented in various Arab and neighboring countries. For example, in Jordan, the figures were 18.1/100,000 for males and 3.8/100,000 for females; in Qatar, the respective rates were 16.7/100,000 for males and 2.5/100,000 for females; Kuwait reported 13.1/100,000 for males and 4.0/100,000 for females [14]. Similarly, in Iran, the figures stood at 15.4/100,000 for males and 5.0/100,000 for females [15]. Notably lower than Lebanon (30.5/100,000 for males and 14.3 for females) [14], Bahrain reported ASIRs of 26.1/100,000 among males and 10.0/100,000 among females [16].

The ASIR of lung cancer incidence exhibited fluctuations based on sex and geographical regions. Turkey registered the highest ASIR among males at 74.9/100,000, followed by Pland-Kiele at 61.0/100,000, and Central and Eastern Europe at 53.5/100,000. In contrast, Eastern Africa recorded the lowest with 3.8/100,000, followed by Middle Africa at 2.0/100,000, and Western Africa at 1.7/100,000. The spectrum varied among females, with Denmark (36.5/100,000), Northern America (33.8/100,000), and Canada (31.9/100,000) reporting the highest ASIRs. On the other end of the spectrum, Turkey (2.0/100,000), Western Africa (1.1/100,000), and Middle Africa (0.8) posted the lowest ASIRs Figure 4.

This study identified an escalating trend in lung cancer incidence within the Iraqi population over the study period, particularly marked by a swifter increase in female lung cancer cases. This parallels international research that has shown a more rapid rise in the prevalence and incidence of lung cancer among female patients [17]–[21]. In comparison to the 50-59-year age group, the ≥60-year age group exhibited the highest number of newly diagnosed lung cancer cases, while the ≤49-year age group showed the fewest instances. Similar patterns have been observed in Lebanon [14], Saudi Arabia [22], and Taiwan [21].

Tobacco smoking remains the foremost major risk factor for lung cancer, supported by compelling evidence [23], [24]. Cigarette smoking habits are strongly associated with lung cancer incidence, mortality, and survival [25], [26]. Smokers face a 30-fold higher risk of developing cancer compared to nonsmokers [23], [24], [27], [28].

In Iraq, tobacco smoking has reached epidemic proportions. The driving forces behind smoking prevalence lie in social, cultural, and posttraumatic stress disorder contexts [29], [30]. Dawood *et al.* [31] reported that many Iraqi smokers possess limited understanding and awareness of the health consequences of smoking, especially among secondhand smokers. A three-year investigation (2005 to 2007) focused on newly diagnosed Iraqi cancer patients recorded by the Iraqi Ministry of Health found lung cancer to be the second most frequent malignancy, comprising 8.43% of all cancer cases and the foremost prevalent site among males [32]. Four studies conducted across five Iraqi provinces (Misan, AL-Diwanyah, Babylon, Erbil, and Duhok) unveiled a notable association between tobacco use and lung cancer prevalence. A study in the Missan province from 2015 to 2016 revealed elevated incidence rates among the age groups of 60-80 years, with males displaying a higher incidence than females. The study further disclosed that 78.15% of the lung cancer population were smokers. Similarly, in the AL-Diwanyah province, Albadri and Alzamily revealed that 70% of lung cancer patients were males, with 96% of them being smokers. Cases correlated with the duration and amount of daily cigarette consumption [11]. In the Babylon governorate, another study showcased a robust correlation between smoking habits and lung cancer occurrences, alongside residing in rural areas and males aged 60 and above [12]. Additionally, M-Amen *et al.* [33] established that a significant risk factor among females in the Duhok governorate is the surge in tobacco smoking, contributing to the heightened incidence of lung cancer there.

The upward trajectory of lung cancer incidence is primarily attributed to factors including extended life expectancy, smoking, radon exposure, environmental influences, sedentary lifestyles, familial cancer history, and genetic components [34]-[36]. However, the scope of the study does not encompass an exploration of why the incidence of lung cancer in Iraq is undergoing an increase or decrease. Among the most addressable challenges are smoking and environmental exposures, which can be tackled through appropriate measures and by raising awareness about their detrimental effects on lung cancer. This, coupled with improvements in case reporting in recent years, may collectively contribute to the upswing in lung cancer cases in Iraq. These findings hold the potential to inform and enhance strategies for lung cancer control, prevention, and early detection in Iraq. Further studies are warranted, building upon the insights gleaned from this work.

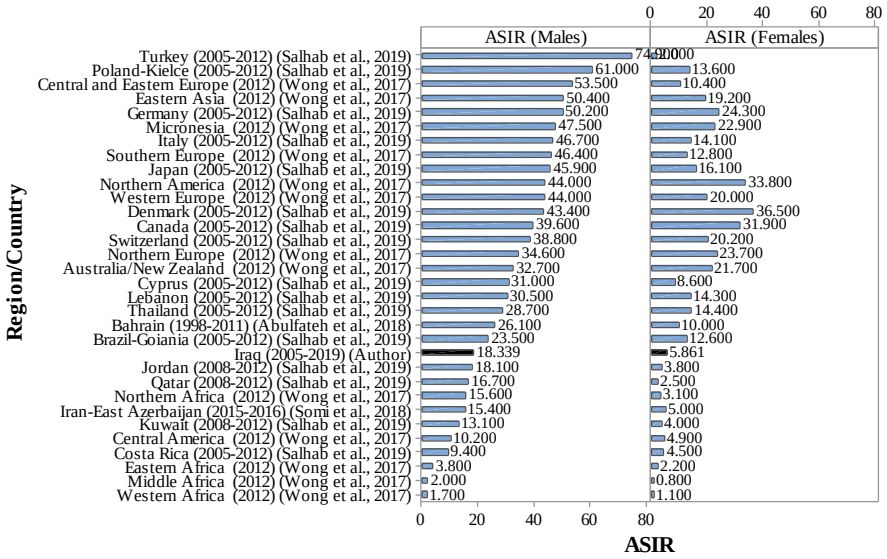

Figure 4. ASIR (1/100,000) of lung cancer for Iraqi males and females compared to other countries

4. CONCLUSION

The study's findings have revealed significant disparities in lung cancer trends, closely aligning with numerous international studies. The prevalence of lung cancer is on an upward trajectory, with females experiencing a notable surge in incidence. This impact is most pronounced among older age groups. These trends underscore the urgent need for coordinated efforts from health policymakers and healthcare practitioners. Addressing and mitigating the risk factors contributing to the persistence of this deadly cancer is imperative. This requires the promotion of early detection strategies and the advocacy for smoking cessation. Furthermore, the study highlights the importance of future research to delve deeper into the underlying risk factors involved.

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BIOGRAPHIES OF AUTHORS

Muzahem M. AL-Hashimi is an assistant professor specializing in applied statistics. He currently holds an academic position in the Department of Statistics and Informatics at the University of Mosul. He has diverse research interests in Epidemiology, Public Health, and the Environment. For more information or inquiries. He can be contacted at email: muzahim_alhashime@uomosul.edu.iq.

Mohammed Qasim Yahya Alawjar is a Lecturer specializing in applied statistics and currently holds an academic position in the Department of Statistics and Informatics at the University of Mosul. He has diverse research interests, including applied statistics, operations research, artificial intelligence, public health, and the environment. For more information or inquiries. He can be contacted at email: mqy.alawjar@uomosul.edu.iq.