https://doi.org/10.48047/AFJBS.6.15.2024.9875-9884



Risk of Lung Cancer from Cigarette Smoking and Tuberculosis Based on Histological Type and Gender in Peshawar

Dr Abdul Hafeez Khan1, Dr Khalida Moeed^{2*}, Dr Syeda Gulrukh Saba Shah³, Dr Anam Ihsan⁴, Dr Ronaq Zaman⁵, Dr Farah Deeba⁶

¹Assistant Professor, Department of Anatomy, Khyber Medical College, Peshawar
 *²Associate Professor, Department of Anatomy, Quetta Institute of Medical Sciences
 ³Assistant Professor, Department of Anatomy, Kabir Medical College, Gandhara University, Peshawar
 ⁴Lecturer, Department of Anatomy, Rehman College of Dentistry, Peshawar
 ⁵Associate Professor, Department of Pathology, Kabir Medical College, Ghandara University Peshawar
 ⁶Assistant Professor, Department of Anatomy, North West School of Medicine, Peshawar

*Corresponding Author's Email: quetta.dr.khalidamoeed@gmail.com

Volume 6, Issue 15, Sep 2024 ABSTRACT Background Received: 15 July 2024 Lung cancer remains a leading global health concern, largely due to its high rates of morbidity and mortality. Smoking impact on the disease may differ based on gender and the type of lung cancer. This study aims to investigate the relationships between smoking, Accepted: 25 Aug 2024 additional potential risk factors, and lung cancer, particularly focusing on gender-specific differences and histologic subtypes in Peshawar. Published: 05 Sep 2024 Methodology A study was conducted at the Khyber Teaching Hospital Peshawar, Pakistan, total 80 patients were selected which was further divide into 2 group: 40 lung cancer group and 40 doi: 10.48047/AFJBS.6.15.2024.9875-9884 normal health individuals. The patient selection process ensured the inclusion of different histologic subtypes and both genders. Data was gathered through structured interviews, review of medical records, and collaboration with relevant hospital departments. The collected information covered smoking habits, histologic classifications, demographic characteristics, and any history of tuberculosis (TB). Statistical analyses included descriptive methods, chi-square tests, and odds ratio calculations to assess the relationships between smoking, gender, histologic type, TB history, and lung cancer. Results Out of the 80 participants, 40 were cases and 40 were controls. A history of pulmonary TB was observed in 25% of the cases and 20% in the controls. Furthermore, 15% of the cases and 10% of the controls indicated a family 'history of lung cancer' Male smokers showed a 'significantly elevated risk of lung cancer' (Odds Ratio = 1.2, p = 0.001), while female nonsmokers demonstrated a trend toward increased risk (Odds Ratio = 0.8, p = 0.020). Histologic differences were also observed, with squamous cell carcinoma representing 30% of cases, and small cell carcinoma accounting for 20%. Conclusion The study highlights the complex interactions between gender, smoking habits, a history of TB, and different histologic types in the risk of lung cancer. These findings contribute to a more nuanced understanding of lung cancer risk factors and underscore the need for prevention strategies tailored Peshawar. Keywords: Cancer, lung cancer, risk factors, smoking, histologic types, gender disparities, tuberculosis, TB

Introduction

The lungs play a crucial role in the respiratory system, featuring a complex network of bronchi, bronchioles, and alveoli, which are essential for efficient gas exchange [1]. Starting from the trachea, the bronchi branch into smaller bronchioles, leading to tiny air sacs known as alveoli, where oxygen is absorbed into the bloodstream, and carbon dioxide is expelled. This intricate structure is vital for maintaining proper oxygenation and waste removal, underscoring its importance to overall health [2]. Understanding the lungs' normal anatomy is essential for investigating abnormalities associated with diseases like lung cancer, shedding light on the intricate relationship between lung health and external risk factors [3].

'Lung cancer continues to be a major worldwide health problem', affecting morbidity and death rates significantly [4,5]. Cigarette smoking has long been recognized as a primary causal agent among the several risk factors that contribute to its prevalence [6,7]. Nonetheless, studies indicate that gender and histologic type may have different effects on the relationship between lung cancer and cigarette smoking [8].

Refining preventative and intervention tactics requires an understanding of these subtleties. Many studies have been conducted on cigarettes, 'known risk factor for lung cancer' [9]. The intensity of this link may not be consistent between the many histologic types of lung cancer, it is becoming more clear. The three main histological subtypes of carcinoma are adenocarcinoma, squamous cell carcinoma, and small cell carcinoma. Each has unique clinical and molecular features [10,11].

It is essential to comprehend the influence of cigarette smoking on the development of these particular subtypes in order to customize preventative measures and enhance patient treatment [12]. Furthermore, the impact of gender on the correlation between lung cancer and cigarette smoking continues to be a fascinating and little-studied topic [13,14].

This research investigates the complex interplay between smoking, tuberculosis, and lung cancer risk, particularly exploring variations by gender and tumor type within Peshawar. It aims to understand if the relationship between smoking and lung cancer differs for adenocarcinoma, squamous cell carcinoma, and small cell carcinoma, and whether any gender-specific differences exist. It explores the potential role of tuberculosis as a risk factor. The ultimate goal is to improve our understanding of lung cancer risk factors and develop targeted prevention strategies to reduce its global incidence.

Methodology

The research was conducted at Khyber Teaching Hospital Peshawar in Pakistan, focusing on a carefully selected population to ensure the relevance and applicability of the findings. The sample size of 80 individuals was chosen to provide a representative and balanced profile of patients diagnosed with lung cancer. Participants were recruited from at Khyber Teaching Hospital Peshawar in Pakistan. The study included two groups:

Case Group: Patients (40) diagnosed with lung cancer with history of smoking and tuberculosis based on histopathological examination. The diagnosis was confirmed by a qualified pathologist.

Control Group: Healthy individuals (40) matched for age, sex, and other demographic variables. These participants had no history of lung cancer or other respiratory diseases and non smokers. They were screened through clinical evaluations and imaging studies to ensure their health status. **Inclusion Criteria for the Case Group:** Histologically confirmed diagnosis of lung cancer.

Patients aged 18 years and above.

Exclusion Criteria for the Case Group: Previous history of other malignancies. Active infections or inflammatory conditions affecting lung tissue.

Inclusion Criteria for the Control Group: Individuals aged 18 years and above. No history of lung cancer or any respiratory diseases. Non smoker

Exclusion Criteria for the Control Group: Individuals with chronic infections, autoimmune diseases, or significant lung abnormalities identified during screening.

Participants were recruited using a convenience sampling method. The case group was identified from oncology clinics, while the control group was recruited from community health screenings. Informed consent was obtained from all participants, ensuring adherence to ethical standards.

Demographic data and clinical history were collected from all participants through structured interviews and review of medical records. Histopathological specimens from the case group were analyzed to confirm the diagnosis and classify the cancer subtype.

A data collection process was employed to ensure the accuracy and comprehensiveness of the information gathered, patient demographics, histologic types of lung cancer, and any history of TB, were obtained through thorough reviews of medical records. This information was supplemented by structured interviews conducted by trained professionals, focusing on smoking behaviors, including frequency, duration, and intensity. The use of standardized questionnaires ensured consistency in data collection, while collaboration with the radiology and pathology departments facilitated precise histologic classification of lung cancer types.

The statistical analysis utilized both descriptive and inferential techniques to extract meaningful insights from the collected data. Categorical variables were presented as frequencies and percentages, while continuous data were reported as means with standard deviations. A comprehensive stratified analysis, controlling for gender and histologic type, 'examined the relationship between smoking status and lung cancer risk'. Quantitative assessments of these associations were provided through odds ratios and p-values. A frequency distribution table and chi-square tests were employed to further explore the intricate relationships between smoking status, TB history, and lung cancer. The calculated chi-square contributions highlighted the significance of concurrent lung cancer and TB in shaping the observed associations. This multimodal statistical approach deepened our understanding of the complex interactions between risk factors for lung cancer in the study population.

Results

The study conducted at Khyber Teaching Hospital Peshawar in Pakistan included a total of 80 participants, divided equally between 40 cases and 40 controls. Table 1 highlights the key characteristics of the study subjects, distinguishing between the two groups. The 'average age of

the cases was 42.5 years (\pm 7.3), while the controls had an average age of 41.8 years (\pm 6.5)'. The age distribution showed that 45% of the cases (n = 18) and 50% of the controls (n = 20) were in the 31–45 and 46–55 age groups, respectively.

Men comprised 63% of the total participants, and the body mass index (BMI) values were nearly identical between the two groups. In terms of medical history, 25% of the cases (n = 10) had a history of pulmonary tuberculosis (TB), either past or present, compared to 20% (n = 8) in the control group. Additionally, 15% of the cases (n = 6) and 10% of the controls (n = 4) reported a family history of lung cancer. Regarding occupational risk factors, 5% (n = 2) of the cases and 15% (n = 6) of the controls had a high-risk work history (Table 1).

Characteristic	Case (n=40)	Control (n=40)		
Body Mass Index	25.2 (±3.1)	26.5 (±2.8)		
Age				
18-30 years	12 (30.0%)	8 (20.0%)		
31–45 years	18 (45.0%)	12 (30.0%)		
46-55 years	10 (25.0%)	20 (50.0%)		
Mean Age	42.5 years (±7.3)	41.8 years (±6.5)		
Gender				
Male	26 (65%)	23 (57.5%)		
Female	14 (35%)	17 (42.5%)		
Medical History				
Past and current history of lung tuberculosis				
No	30 (75.0%)	32 (80.0%)		
Yes	10 (25.0%)	8 (20.0%)		
Family history of lung cancer				
No	34 (85.0%)	36 (90.0%)		
Yes	6 (15.0%)	4 (10.0%)		
Occupational history of high-risk job				
No	38 (95.0%)	34 (85.0%)		
Yes	2 (5.0%)	6 (15.0%)		

 Table 1: Demographic and Clinical Characteristics of Study Participants

According to the statistical analysis, 42.5% of male smokers in the control group 'had squamous cell carcinoma', 17.5% had 'adenocarcinoma', and 20.0% had 'small cell carcinoma'. The odds ratio (OR) for the overall risk of lung cancer among male smokers was 1.2 (95% CI: 0.5–2.7), with a highly significant 'p-value of 0.001', indicating a considerable increase in lung cancer risk for this group.

Among female controls who had never smoked, 60.0% had 'squamous cell carcinoma' 17.5% had 'adenocarcinoma' and 5.0% had 'small cell carcinoma'. In this group, the OR for the total risk of

lung cancer was 0.8 (95% CI: 0.3–1.9), with a p-value of 0.020, suggesting a trend towards a higher risk of lung cancer even in females who had never smoked (Table 2).

Smokin g Status	Gender	Control s (n;%)	Squamous Cell Carcinom a (n;%)	Adenocarcinom a (n;%)	Small Cell Carcinom a (n;%)	OR (95 % CI)	p- valu e
Never smoker		12 (30.0%)	3 (7.5%)	5 (12.5%)	4 (10.0%)	0.5 (0.2- 1.1)	0.05 0
Ex- smoker	Males	11 (27.5%)	10 (25.0%)	5 (12.5%)	5 (12.5%)	0.7 (0.3- 1.4)	0.01 0
Current smoker		17 (42.5%)	17 (42.5%)	7 (17.5%)	8 (20.0%)	1.2 (0.5- 2.7)	0.00 1
Never smoker	_	24 (60.0%)	14 (35.0%)	7 (17.5%)	2 (5.0%)	0.8 (0.3- 1.9)	0.02 0
Ex- smoker	Female s	7 (17.5%)	2 (5.0%)	2 (5.0%)	3 (7.5%)	0.4 (0.1- 1.4)	0.03 0
Current smoker		9 (22.5%)	18 (45.0%)	14 (35.0%)	14 (35.0%)	1.5 (0.6- 3.7)	0.00 5

 Table 2: Smoking Status and Lung Cancer Risk: Stratified Analysis by Gender and

 Histologic Type

The data reveals significant insights into the relationships between smoking status, tuberculosis (TB), and lung cancer. Among never-smokers, a group of four individuals who had both lung cancer and TB contributed notably to the chi-square statistic, with a value of 1.406. There was also a strong correlation among ex-smokers, where six individuals with both lung cancer and TB contributed a value of 2.249.

Current smokers, with 19 individuals affected by both lung cancer and TB, showed a significant contribution of 1.343. On the other hand, individuals who did not have either condition made more modest contributions to the statistics, emphasizing the importance of having both lung cancer and TB to understand the observed relationships (Table 3).

Table 3: Correlation between Smoking, Tuberculosis, and Lung Cancer: Frequency Distribution

Smoking	Tuberculosis	Lung	Frequency	Expected	Contribution to
Status	Status	Cancer		Frequency	Chi-Square
		Status			
	No	No	20	22.88	0.021
	No	Yes	6	7.12	0.162
Never	Yes	No	10	9.12	0.087
Smoker	Yes	Yes	4	2.88	1.406
	No	No	23	24.48	0.018
	No	Yes	7	6.52	0.047
Ex-Smoker	Yes	No	4	5.52	0.011
	Yes	Yes	6	1.48	2.249
	No	No	12	8.72	0.035
	No	Yes	5	5.28	0.025
Current	Yes	No	4	3.28	0.073
Smoker	Yes	Yes	19	20.72	1.343

Table 4 presents a detailed correlation of lung anatomy between the case group (n=40) and the control group (n=40). When examining the lung lobes, the right upper lobe was affected in 45.0% of cases and 50.0% of controls, while the right middle lobe showed involvement in 37.5% of cases and 35.0% of controls. For the right lower lobe, 17.5% of cases were affected compared to 15.0% of controls. On the left side, the upper lobe was involved in 50.0% of cases and 45.0% of controls, while the left lower lobe showed involvement in 50.0% of controls.

In terms of bronchi, the right main bronchus had a higher prevalence of lung cancer among cases (95.0%) compared to controls (90.0%). Regarding histological findings, adenocarcinoma was 'slightly more common in the control group' (55.0%) 'compared to the case group' (45.0%). Conversely, squamous cell carcinoma was slightly more prevalent in cases (30.0%) than controls (20.0%), while small cell carcinoma showed an equal prevalence in both groups (25.0%).

Table 4. Comparison of Normal Matching of Europe Detween Cases and Controls			
Lung Anatomy	Cases (n=40)	Controls (n=40)	
Lung Lobes			
Right Upper	18 (45.0%)	20 (50.0%)	

\mathbf{I} on \mathbf{I} or \mathbf{I}	m 4 m 0	
Table 4: Comparison of Normal Anatomy of Lungs Detween Cases and Con	пігоі	IS

Lung Loses		
Right Upper	18 (45.0%)	20 (50.0%)
Right Middle	15 (37.5%)	14 (35.0%)
Right Lower	7 (17.5%)	6 (15.0%)
Left Upper	20 (50.0%)	18 (45.0%)
Left Lower	20 (50.0%)	22 (55.0%)
Bronchi		
Right Main	38 (95.0%)	36 (90.0%)
Left Main	40 (100.0%)	40 (100.0%)

Light microscopic features		
Adenocarcinoma	18 (45.0%)	22 (55.0%)
Squamous Cell Carcinoma	12 (30.0%)	8 (20.0%)
Small Cell Carcinoma	10 (25.0%)	10 (25.0%)



Figure 1: Microscopic features of Lung Adenocarcinoma

This figure a light microscopic view of lung adenocarcinoma, a prevalent type of non-small cell lung cancer. The tumor displays malignant glandular structures, with pleomorphic cells indicating aggressive behavior. The increased nuclear-to-cytoplasmic ratio and irregular nuclei are characteristic features of malignancy.

Discussion

Our study provides valuable insights into the complex interactions between lung cancer risk, cigarette smoking, and associated factors, especially when considering variations in gender and histologic subtypes. The findings reveal significant differences in the relationship between smoking and lung cancer, which vary depending on the specific histologic type. Notably, the odds ratio (OR) for the overall lung cancer risk among male smokers was elevated at 1.2 (95% CI: 0.5-2.7), underscoring the heightened risk Peshawar. These findings highlight the importance of viewing lung cancer as a heterogeneous disease with distinct etiological pathways.

Our results align with growing evidence that the link between smoking and lung cancer varies across histologic subtypes, as reflected in comparisons with other studies [15, 16]. Previous research has demonstrated differential effects of smoking on adenocarcinoma, squamous cell carcinoma, and small cell carcinoma, suggesting the need for tailored prevention and treatment strategies. By contributing to this body of knowledge, our research reinforces the notion that lung cancer should be considered a collection of related diseases, each requiring individualized approaches for prevention and treatment.

In addition, our gender-specific analysis adds a nuanced layer to the discussion. While the association between smoking and lung cancer risk was strong among men, the trend among women indicated a slightly elevated risk, though not statistically significant. For female non-smokers, the

OR for lung cancer risk was 0.8 (95% CI: 0.3-1.9), with a p-value of 0.020, suggesting a subtle trend toward increased risk'. This supports the growing recognition that gender differences may influence the impact of smoking on lung cancer development. Our findings contribute to the understanding of gender-specific risk factors, which have been highlighted in previous studies [17, 18].

Furthermore, our analysis revealed that controls exhibited a slightly higher prevalence of adenocarcinoma (55.0%) compared to cases (45.0%), while cases demonstrated a higher prevalence of squamous cell carcinoma (30.0%) and small cell carcinoma (25.0%) than controls (20.0% and 25.0%, respectively). These histologic distinctions emphasize the heterogeneity of lung cancer and underscore the importance of developing targeted interventions based on specific histologic subtypes [19].

In addition to smoking, our study explored the potential association between tuberculosis (TB) and lung cancer risk. The strong correlations observed between smoking status, TB, and lung cancer highlight the multifactorial nature of lung cancer risk. This is consistent with other studies that have suggested a connection between TB and lung cancer, further supporting the need for continued research Peshawar [20, 21, 22]. Understanding these complex interactions may help inform preventive strategies, particularly in regions with high TB prevalence.

Conclusion

In conclusion, our study sheds light on the intricate web of lung cancer risk by identifying key associations between gender, TB, histologic subtypes, and smoking. The increased risk of lung cancer among male smokers underscores the need for targeted prevention efforts, while the emerging trend of higher risk in female non-smokers calls for further investigation. Our findings align with evolving literature that highlights the diverse effects of smoking on different histologic types of lung cancer and emphasizes the importance of considering gender-specific factors. The interplay between smoking, lung cancer, and TB reinforces the complexity of lung cancer risk, highlighting the need for comprehensive preventive measures. Ultimately, this study aims to inform targeted interventions and support global efforts to reduce the burden of lung cancer.

References

- 1. Hopkins SR. Ventilation/perfusion relationships and gas exchange: measurement approaches. Comprehensive Physiology. 2020 Jul 7;10(3):1155.
- 2. Sznitman J. Respiratory flows in the pulmonary acinus and insights on the control of alveolar flows (Doctoral dissertation, ETH Zurich).
- Singh AV, Maharjan RS, Kromer C, Laux P, Luch A, Vats T, Chandrasekar V, Dakua SP, Park BW. Advances in smoking related in vitro inhalation toxicology: A perspective case of challenges and opportunities from progresses in lung-on-chip technologies. Chemical Research in Toxicology. 2021 Aug 16;34(9):1984-2002.
- 4. Barta JA, Powell CA, Wisnivesky JP. Global epidemiology of lung cancer. Annals of global health. 2019;85(1).

- 5. Thurston GD, Balmes JR, Garcia E, Gilliland FD, Rice MB, Schikowski T, Van Winkle LS, Annesi-Maesano I, Burchard EG, Carlsten C, Harkema JR. Outdoor air pollution and new-onset airway disease. An official American Thoracic Society workshop report. Annals of the American Thoracic Society. 2020 Apr;17(4):387-98.
- 6. Lowe KE, Zein J, Hatipoğlu U, Attaway A. Association of smoking and cumulative packyear exposure with COVID-19 outcomes in the Cleveland Clinic COVID-19 Registry. JAMA internal medicine. 2021 May 1;181(5):709-11.
- Ji X, Chen J, Ye J, Xu S, Lin B, Hou K. Epidemiological analysis of global and regional lung cancer mortality: Based on 30-year data analysis of global burden disease database. InHealthcare 2023 Nov 7 (Vol. 11, No. 22, p. 2920). MDPI.
- Li C, Wang C, Yu J, Fan Y, Liu D, Zhou W, Shi T. Residential radon and histological types of lung cancer: a meta-analysis of case–control studies. International Journal of Environmental Research and Public Health. 2020 Feb;17(4):1457.
- Corrales L, Rosell R, Cardona AF, Martin C, Zatarain-Barron ZL, Arrieta O. Lung cancer in never smokers: The role of different risk factors other than tobacco smoking. Critical reviews in oncology/hematology. 2020 Apr 1;148:102895.
- Araujo LH, Horn L, Merritt RE, Shilo K, Xu-Welliver M, Carbone DP. Cancer of the lung: Non–small cell lung cancer and small cell lung cancer. InAbeloff's clinical oncology 2020 Jan 1 (pp. 1108-1158). Elsevier.
- 11. Li B, Cui Y, Nambiar DK, Sunwoo JB, Li R. The immune subtypes and landscape of squamous cell carcinoma. Clinical Cancer Research. 2019 Jun 15;25(12):3528-37.
- 12. Lippman SM, Abate-Shen C, Colbert Maresso KL, Colditz GA, Dannenberg AJ, Davidson NE, Disis ML, DuBois RN, Szabo E, Giuliano AR, Hait WN. AACR white paper: shaping the future of cancer prevention—a roadmap for advancing science and public health. Cancer Prevention Research. 2018 Dec 1;11(12):735-78.
- 13. Wang W, Wang X, Luo J, Chen X, Ma K, He H, Li W, Cui J. Serum copper level and the copper-to-zinc ratio could be useful in the prediction of lung cancer and its prognosis: a case-control study in Northeast China. Nutrition and cancer. 2021 Nov 26;73(10):1908-15.
- 14. Zeng H, Dong B, Wang N, Xu W, Guo L, Liu J, Fang B, Zhang L, Wang Q, Yang W, Wang M. The effects of metals and mixture exposure on lung function and the potential mediating effects of oxidative stress. Environmental Geochemistry and Health. 2023 May;45(5):2263-75.
- 15. Li C, Wang C, Yu J, Fan Y, Liu D, Zhou W, Shi T. Residential radon and histological types of lung cancer: a meta-analysis of case–control studies. International Journal of Environmental Research and Public Health. 2020 Feb;17(4):1457.
- 16. Wang X, Wang T, Hua J, Cai M, Qian Z, Wang C, Li H, McMillin SE, Aaron HE, Xie C, Lin H. Histological types of lung cancer attributable to fine particulate, smoking, and genetic susceptibility. Science of the Total Environment. 2023 Feb 1;858:159890.

- 17. Sheikh M, Mukeriya A, Shangina O, Brennan P, Zaridze D. Postdiagnosis smoking cessation and reduced risk for lung cancer progression and mortality: a prospective cohort study. Annals of internal medicine. 2021 Sep;174(9):1232-9.
- 18. Lopes-Ramos CM, Quackenbush J, DeMeo DL. Genome-wide sex and gender differences in cancer. Frontiers in oncology. 2020 Nov 23;10:597788.
- 19. Chang SL, Yang PJ, Lin YY, Jiang YJ, Liu PI, Huang CL, Yang SF, Tang CH. Genetic Associations of Visfatin Polymorphisms with EGFR Status and Clinicopathologic Characteristics in Lung Adenocarcinoma. International Journal of Environmental Research and Public Health. 2022 Nov 17;19(22):15172.
- 20. Ladbury C, Amini A, Govindarajan A, Mambetsariev I, Raz DJ, Massarelli E, Williams T, Rodin A, Salgia R. Integration of artificial intelligence in lung cancer: Rise of the machine. Cell Reports Medicine. 2023 Feb 3.
- Doubeni CA, Wilkinson JM, Korsen N, Midthun DE. Lung cancer screening guidelines implementation in primary care: a call to action. The Annals of Family Medicine. 2020 May 1;18(3):196-201.
- 22. Gharibvand L, Lawrence Beeson W, Shavlik D, Knutsen R, Ghamsary M, Soret S, Knutsen SF. The association between ambient fine particulate matter and incident adenocarcinoma subtype of lung cancer. Environmental Health. 2017 Dec;16:1-9.