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Association of Disease Outcome with Diabetes in Lung Cancer Patients

Amina Abid[1], Ayaz Arshad[2], Muhammad Arslan[3]

[1]Department of Internal Medicine, Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Punjab, Pakistan.
[2]Department of Cardiology, Mujahid Heart Center, Lahore, Punjab, Pakistan.
[3]Department of Internal Medicine, Mujahid Hospital, Lahore, Punjab, Pakistan.

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Correspondence to: Amina Abid, Department of Internal Medicine, Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Punjab, Pakistan.
Email: aminaabid1014@gmail.com

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ABSTRACT

Objective: To determine the frequency of diabetes in patients with lung cancer and to compare the frequency of mortality with diabetes in lung cancer patients. **Methodology:** This study was descriptive case series carried out at department of Medicine, Shaukat Khanum Memorial Cancer Hospital & Research Center Lahore. The duration of the study was six months from January 2024 to June 2024. After meeting selection criteria and applying non-probability convenient sampling 100 patients were enrolled. Informed consent and demographic details were taken. From all the lung cancer patients, history of diabetes was noted. All patients were followed up in medical wards for 3 months. If patient died during treatment, then mortality was labeled as outcome. **Results:** The mean age of the patients was 50.78±11.57 years and 61% patients were males. Among lung cancer patients 33% were diabetics and mortality during treatment was noted in 46% patients. In diabetics, mortality during treatment was found in 18(54.5%) patients and in non-diabetics it was observed in 28(41.8%) patients (p-value=0.229). **Conclusion:** This study concluded that one-third of lung cancer patients had diabetes mellitus, and 46% experienced mortality during treatment. Moreover, no statistically significant association was found between the presence of diabetes mellitus and mortality during the treatment of lung cancer patients.

INTRODUCTION

Among the most frequent diseases and the major cause of cancer fatalities, lung cancer accounts for 18% of deaths in men and women. [1, 2] The kidney, retina, and vascular system may all be impacted by diabetes mellitus, a systemic disease marked by hyperglycemia, inflammation, and oxidative stress. [3-5] Diabetes mellitus may potentially impact lung cancer via processes, such as hyperinsulinemia, hyperglycemia, or chronic inflammation, which have been related with cancer development. [6, 7] The cardiovascular and neurological systems are particularly vulnerable to elevated blood sugar. Diabetes is connected to dementia, hearing loss, and some cancers, according to recent research. Diabetes increases cancer risk and death and may affect cancer development and prognosis. All-cause mortality in cancer patients is also linked to diabetes. [8, 9] Patients with lung cancer have a high frequency of comorbidity. [10] The survival rate of cancer mostly relies on patient features, tumor histology and pathology, stage at diagnosis, host-tumor interactions, and comorbidities. Comorbidity inherently affects each patient's first therapy and the efficacy of patient care. [11]

Diabetes increases the chance of cancer-related mortality; however, it is unclear whether this risk has altered or what forms of cancer are causing it. [12] Previous research revealed that diabetes mellitus is related to cancer risk and mortality, but studies addressing the association between diabetes mellitus and lung cancer prognosis remain disputed. [13] Diabetes has been associated with various malignancies, including breast, pancreatic, and liver cancer. Type 2 diabetes, accounting for over 90% of global cases, is linked to hyperinsulinemia and hyperglycemia, both of which are recognized as promoters of tumor cell proliferation. Cancer cells exhibit a greater reliance on glucose metabolism for proliferation compared to non-cancer cells. Hyperinsulinemia promotes cancer cell growth both directly via the insulin receptor and indirectly through insulin-like growth factor 1 (IGF-1) and its receptor (IGF-1R). [14, 15]

The relationship between diabetes mellitus and lung cancer risk remains contentious, with certain studies indicating an elevated risk of lung cancer associated with

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diabetes, while others suggest a reduced risk. The risk factors for various malignancies that coexist with diabetes mellitus include central adiposity and chronic inflammation. [16, 17] Total BMI exhibits an inverse relationship with lung cancer risk; however, waist circumference, indicative of central adiposity, shows a positive association with risk. Outcome data regarding the survival of patients with concurrent lung cancer and diabetes mellitus are inconsistent. [10, 18] Therefore, research on our community is necessary, as is evidence for the local population since diabetes mellitus is already quite common in Pakistan and may have a negative impact on prognosis. Therefore, this study's goal was to ascertain the prevalence of diabetes in lung cancer patients and assess the prevalence of diabetes-related mortality in lung cancer patients.

MATERIAL AND METHODS

It was a descriptive case series that was carried out at the department of Medicine, Shaukat Khanum Memorial Cancer Hospital & Research Center Lahore. The duration of the study was six months from January 2024 to June 2024. 100 lung cancer patients were included in this study using non-probability convenient sampling technique. Patients having an age range between 25-65 years of either gender diagnosed with lung cancer were included. Patients with distant metastasis, lung cancer of unknown pathological type, unclear staging, or exhibited non-squamous cell lung carcinoma histology (on medical record) fell in exclusion criteria. The diagnosis of lung cancer was confirmed based on the presence of squamous cell carcinoma in the lungs, as determined through histopathology. Diabetes mellitus was defined as a blood glucose level exceeding 186 mg/dL for more than one year and an HbA1c greater than 6.5% prior to the diagnosis of lung cancer. Ethical approval was taken from the institutional ethical board. After meeting selection criteria informed consent and demographic detail was taken from all the patients. From all the lung cancer patients, history of diabetes was noted. Patients were managed as per standard protocol. All patients were followed up in medical wards for 3 months. If patient died during treatment, then mortality was labeled as outcome. All the data was recorded in Performa while it was analyzed in SPSS 25. The Chi-square test was applied to compare mortality in patients with or without diabetes, keeping P-value≤0.05 as significant.

RESULTS

In this study, 100 lung cancer patients participated. The mean age, BMI, and duration of lung cancer of the patients was 50.78±11.57 years, 27.08±4.27 Kg/m2 and 11.33±5.08 months, respectively. Out of 100 patients 61% were males and 39% were females. Male to female ratio of the patients was 1.5:1. In this study 30% of patients were smokers, 50% were hypertensive and family history of cancer was noted in 17(17%) patients. In this study 65% of patients had sedentary lifestyle and 27% were stay-at-home spouses. Among lung cancer patients 33% were diabetics **(Table 1)**. According to this study, lung cancer patients' mortality during treatment was observed in 46% of patients **(Fig 1)**. In male patients' mortality during treatment was noted in 27 (44.3%) and in females it was noted in 19(48.7%) patients (p-value=0.663). Among smokers' mortality during treatment was found in 14(46.7%) patients and in non-smokers it was observed in 32(45.7%) patients (p-value=0.930). Hypertension was significantly associated with mortality during treatment of the patients. In hypertensive patients' mortality during treatment was found in 28(56.0%) patients and in non-hypertensive patients it was observed in 18(36.0%) patients (p-value=0.045). Patients on chemotherapy mortality during treatment was noted in 21(42%) patients as compared to patients on radio therapy and combination it was noted in 23(52.3%) & 2(33.3%) patients respectively (p-value=0.495). Diabetes mellitus did not show a significant association between mortality during treatment of the patients. In diabetics, mortality during treatment was found in 18(54.5%) patients and in non-diabetics it was observed in 28(41.8%) patients (p-value=0.229). Similarly, age and BMI comparison between mortality during treatment also showed statistically insignificant difference **(Table 2)**.

Table 1

Descriptive analysis of demographic and clinical variables

Variables	Categories	Frequency
Age (Years)		50.78±11.57 (30.0-70.0)
Gender	Male	61 (61%)
	Female	39 (39%)
BMI (Kg/m2)		27.08±4.27 (20.0-35.0)
Duration of lung cancer		11.33±5.08 (3.0-19.0)
Smoking	Yes	30 (30%)
	No	70 (70%)
Diabetes	Yes	33 (33%)
	No	67 (67%)
Hypertension	Yes	50 (50%)
	No	50 (50%)
FH of cancer	Yes	17 (17%)
	No	83 (83%)
Lifestyle	Active	35 (35%)
	Sedentary	65 (65%)
Occupation	Business	9 (9%)
	Govt. Job	26 (26%)
	Housewife	27 (27%)
	Private	37 (37%)
	Retired	1 (1%)
Treatment receiving for cancer	Chemotherapy	50 (50%)
	Radiotherapy	44 (44%)
	Combination	6 (6%)

Figure 1

Frequency distribution of mortality during treatment

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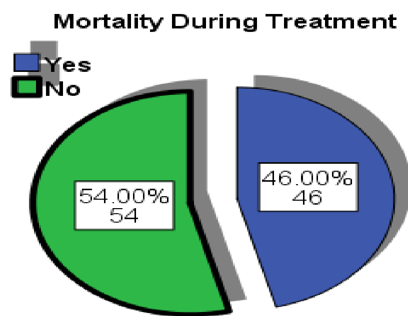

Table 2

Comparison of mortality during treatment between diabetes mellitus and other socio health related factors

		Mortality During Treatment		Total	p-value
		Yes	No		
Age	≤50 years	17(40.5%)	25(59.5%)	42(100.0%)	0.346
	>50 years	29(50.0%)	29(50.0%)	58(100.0%)	
Gender	Male	27 (44.3%)	34(55.7%)	61(100.0%)	0.663
	Female	19(48.7%)	20(51.3%)	39(100.0%)	
BMI	≤25 kg/m^2	17(45.9%)	20(54.1%)	37(100.0%)	0.993
	>25 kg/m^2	29(46.0%)	34(54.0%)	63(100.0%)	
Smoking	Yes	14(46.7%)	16(53.3%)	30(100.0%)	0.930
	No	32(45.7%)	38(54.3%)	70(100.0%)	
Diabetes	Yes	18(54.5%)	15(45.5%)	33(100.0%)	0.229
	No	28(41.8%)	39(58.2%)	67(100.0%)	
Hypertension	Yes	28(56.0%)	22(44.0%)	50(100.0%)	0.045
	No	18(36.0%)	32(64.0%)	50(100.0%)	
FH of cancer	Yes	12(70.6%)	5(29.4%)	17(100.0%)	0.026
	No	34(41.0%)	49(59.0%)	83(100.0%)	
Lifestyle	Active	15(42.9%)	20(57.1%)	35(100.0%)	0.644
	Sedentary	31(47.7%)	34(52.3%)	65(100.0%)	
Occupation	Housewife	13(48.1%)	14(51.9%)	27(100.0%)	0.793
	Others	33(45.2%)	40(54.8%)	73(100.0%)	
Treatment receiving for Cancer	Chemotherapy	21(42.0%)	29(58.0%)	50(100.0%)	0.495
	Radiotherapy	23(52.3%)	21(47.7%)	44(100.0%)	
	Combine	2(33.3%)	4(66.7%)	6(100.0%)	

DISCUSSION

Diabetes is a recognized risk factor for various malignancies, such as hyperglycemia and hyperinsulinemia, which are characteristic of diabetes pathogenesis, and are known to promote tumor growth. [19] Preclinical studies indicate that hyperglycemia enhances the proliferation and invasiveness of lung tumor cells in lung cancer. Hyperglycemia and diabetes may differentially affect various histologic subtypes of lung cancer. In vitro studies indicate that squamous cell carcinoma exhibits a greater dependence on glucose metabolism for growth relative to other subtypes. Individuals consuming high glycemic index diets exhibit an increased risk of squamous cell carcinoma of the lung, while no such association is observed with adenocarcinoma. [20, 21]

Amanda Leiter et al. found 140,395 individuals in our analysis. Diabetes did not affect lung cancer incidence [IRR: 1.03, 95% CI: 0.91–1.17]. Stratified analysis similarly found no significant diabetes-lung cancer risk relationship (all P values >0.05). Diabetes did not independently predict lung cancer in a large PLCO sample. [15] Research found 25% of 203 patients had diabetes. Diabetics had lower median progression-free and overall survival than non-diabetics (5.9 vs. 7.1 months, p = 0.004 and 12 vs. 21 months (about 2 years), p = 0.006). [22]

Another study found 11.11% of 2484 lung cancer patients were diabetic. The mortality rate was 72.8% for diabetics and 73.5% for non-diabetics (p>0.05). [23] According to different research, 7.5% of patients had diabetes, and the death rate for diabetics was 69.5%, while the rate for non-diabetics was 76.8% (p>0.05). [24]

On the other hand, some studies suggest that cancer risk may be highest in the years immediately following diabetes diagnosis. [25, 26] According to different research, those with diabetes mellitus who also have lung cancer had a higher chance of surviving than those who do not. Lung cancer patients with and without diabetes mellitus had respective 1-, 2-, and 3-year survival rates of 43% vs 28%, 19% compared to 11%, and 3% versus 1%. [27] According to data from another study, diabetes mellitus is linked to a higher risk of lung cancer and a lower chance of survival. In addition to having a protective effect on the pathophysiology of lung cancer, metformin is linked to a longer progression-free survival for diabetic lung cancer patients. Human insulin use and the risk of lung cancer are significantly correlated. [28]

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As contradictory findings were observed between our study findings and few of previously published studies, so it is suggested that in future further studies should be done with larger sample size and data must be taken from multicenter setting to control the bias. In this way we can evaluate the findings of our study and can generalize the results to the entire population.

CONCLUSION

This study concluded that one-third of lung cancer patients had diabetes mellitus, and 46% experienced mortality during treatment. Moreover, no statistically significant association was found between the presence of diabetes mellitus and mortality during the treatment of lung cancer patients.

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