RESEARCH ARTICLE

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Association of the -4719A/T Polymorphism in the *RAD51* Gene with Demographic and Clinicopathological Features of Lung Cancer in Iraqi Patients

Zahraa Muhammed Jabur, Rand Mohammed Abdul-Hussein*

Abstract

Introduction: DNA damage and repair (DDR) mechanisms are crucial for maintaining genomic stability by counteracting genetic insults that occur continuously in living organisms. Impairments in DDR pathways can lead to the accumulation of mutations and contribute to carcinogenesis. Lung cancer (LC) remains one of the most prevalent and lethal malignancies worldwide, affecting both men and women. This study aimed to investigate the association between the *RAD51* -4719A/T (rs2619679) single nucleotide polymorphism (SNP) and lung cancer susceptibility. It also examined the correlation between *RAD51* SNP genotypes and demographic, clinical, and pathological features in a cohort of Iraqi patients. **Materials and Methods:** This case-control study consisted of fifty healthy individuals and one hundred and five lung cancer patients. Genotyping of the *RAD51* gene -4719A/T polymorphism was performed using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) analysis. **Results:** Lung cancer was significantly more frequent among older patients (aged 60–69 years), males, and smokers ($p \leq 0.01$). A statistically significant association was found between the *RAD51* -4719A/T polymorphism and lung cancer risk. Individuals carrying the AT and TT genotypes were observed to have a significantly higher frequency of lung cancer compared to those with the AA genotype, highlighting the potential role of this polymorphism in disease susceptibility (χ^2 =127.68, p =0.00000001). Furthermore, the T allele of this SNP was found to be significantly more frequent in lung cancer patients than in controls (p = 0.00000001), suggesting a potential role in increased genetic susceptibility to lung cancer. **Conclusions:** This study is among the first to investigate the −4719A/T (rs2619679) polymorphism in the *RAD51* gene and its association with lung cancer in the Iraqi population. A statistically significant association was identified between this variant and lung cancer risk. The genotypic patterns identified suggest that the presence of the T allele particularly in the more frequently occurring heterozygous AT genotype may contribute to the molecular mechanisms involved in lung cancer development through its impact on DNA repair processes.

Keywords: Lung cancer- *RAD51* gene- single nucleotide polymorphism- PCR-RFLP.

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Introduction

Lung cancer (LC) is one of the most common types of cancer, and a significant number of people die from it each year. Due to the prevalence of late diagnoses, treatment options are often limited [1]. An elevated risk of lung cancer is linked to a number of conditions. Lung cancer is mostly caused by tobacco usage. In addition to air pollution, occupational exposure, and poor diet, additional variables, such as polymorphisms in genes, may potentially change the risk of lung cancer either alone or in conjunction with smoking status to affect the demography of lung cancer [2-4]. Two major categories can be used to classify lung cancers: Lung tumors that are small cell (SCLC) or non-small cell (NSCLC). NSCLC comes in three main forms: lung adenocarcinoma, which accounts for over 40% of all occurrences of lung cancer; squamous cell lung cancer, also known as epidermoid carcinoma, which accounts for roughly 30% of all cases of lung cancer; and large cell lung cancer, which accounts for roughly 10% to 15% of all cases of lung cancer. Adenosquamous carcinoma and sarcomatoid carcinoma are two of the less prevalent kinds of non-small cell lung cancer [5-7].

DNA repair plays a vital role in maintaining cell and tissue balance, responding to both internal and external DNA damage. Any defects in DNA repair can lead to the accumulation of genetic changes, increasing the risk of cancer [8]. One of the most dangerous genomic lesions is double-stranded DNA breaks (DSBs), which, if untreated, can result in cell death and genome rearrangements. DSBs can occur as a result of endogenous processes like meiosis and replication forks running into single strand breaks, or external causes like ionizing radiation (IR). Both

*Department of Biology, Faculty of Science, University of Kufa, Iraq. *For Correspondence: rand.alhusseini@uokufa.edu.iq*

eukaryotic and prokaryotic species use non-homologous end joining (NHEJ) and homologous recombination (HR) as their primary methods for repairing damaged DNA and restoring genomic integrity when DSBs occur. The type of DNA damage, the cell type, and the availability of a second copy of the genetic information all influence which of the two methods is best [9]. A DNA repair protein called RADiation sensitive protein 51 (*RAD51*) contributes to tumor cells' resistance to radiation and chemotherapy and lessens the therapeutic impact [10]. The *RAD51* gene, which has 339 amino acids, is found on chromosome 15q15.1. The *RAD51* is a homolog of Saccharomyces cerevisiae and Escherichia coli RecA [11]. This study was investigated the potential roles of *RAD51* -4791A/T SNP in lung cancer patients and assess the correlation between the *RAD51* -4791A/T SNP and demographic and clinicopathological features of Iraqi patients with lung cancer like sex, age, smoking status, family history, histological subtype of lung cancer, stage, grade of lung cancer and lymph node metastases.

Materials and Methods

Study group

This case-control study was conducted from January 2023 to May 2025 in the Laboratory of Molecular Biology, at Department of Biology, Faculty of Science, University of Kufa, Iraq. Peripheral blood samples were obtained from 105 Iraqi patients diagnosed with lung cancer at the National Hospital for Oncology and Hematology in Najaf Governorate, Iraq. Demographic information-including sex, age, and smoking status-was collected from patients using a structured questionnaire. Clinical data, including histological type, stage, grade of lung cancer, and lymph node metastasis, were obtained from hospital records. The study also included a control group of 50 healthy individuals matched with the patients by age. These controls were selected according to rigorous inclusion criteria to eliminate potential confounding factors. Individuals with any clinical indications of disease, inflammatory conditions, or a personal or first-degree family history of cancer were excluded. This stringent selection aimed to minimize genetic and environmental influences that could bias the comparison between case and control groups.

DNA Isolation

Peripheral blood specimens were collected in EDTA-containing tubes from both patients and controls. Genomic DNA was extracted from blood samples utilizing a specialized commercial kit (Geneaid Biotech, Taiwan), specifically for purifying high-quality DNA from whole blood. DNA concentration was measured using a Nanodrop spectrometer (Biodrop, USA), with absorbance readings at 260/280 nm to assess both concentration (ng/µL) and purity according to Ausubel et al. [12].

Genotyping

The -4791A/T polymorphism of the *RAD51*gene was determined by PCR-RFLP methods. The following primers were used for the PCR amplification: forward 5' CCGTGCAGGCCTTATATGAT-3' and the reverse primer: 5'-AGATAAACCTGGCCAACGTG-3' , as previously described [13]. A total of 2 µl from each primer (forward and reverse) and 5 µl of template DNA were added to AccuPower® TLA PCR PreMix tubes (Bioneer Corporation , Korea).To reach a final reaction volume of 20 µl, nuclease-free water (Promega, USA), certified to be free of DNase and RNase contamination, was added. The PCR amplification was carried out with an initial denaturation step at 95°C for 5 minutes, followed by 30 cycles of denaturation at 95°C for 30 seconds, annealing at 60°C for 45 seconds, and extension at 72°C for 1 minute. A final extension step was performed at 72°C for 5 minutes.

For the restriction fragment length polymorphism (RFLP) analysis, 5 µl of the PCR product was mixed with 0.5 µl of HinfI enzyme (New England BioLabs, Inc, USA), 2.5 µl of 10X NE Buffer, and nuclease-free water to a final volume of 25 µl. The digestion mixture was incubated at 37°C for 15 minutes, followed by enzyme inactivation at 80°C for 20 minutes. The digested fragments were then separated and visualized on a 1% agarose gel through electrophoresis. Genotyping results were interpreted based on fragment sizes: samples with the AA genotype yielded two bands of 286 bp and 116 bp, TT genotypes displayed bands at 172 bp,116 and 114 bp, while heterozygous AT genotypes showed these fragments—286 bp, 172 bp, 116 and 114 bp.

Bio Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS), version 23. The Chi-square test was applied to compare results between the two groups and determine any significant relationships between categorical variables, with a significance level set at $p \leq 0.05$ and $p \leq 0.01$. Results are presented as percentages and case counts.

Results

Characteristics of the study subjects

Analysis of demographic data revealed significant differences in sex, age, and smoking status among the study subjects. The median age at diagnosis was 63.68± 10.32 years (range: 42–89 years), with the largest proportion of patients ($p = 0.000001$) in the 65–69 age group. Among the patients, 34 (32.38%) were females, and 71 (67.62%) were males, showing a significant association between lung cancer and male sex ($p = 0.0003$). Smoking status showed that 59 (56.19%) were smokers, 37 (35.24%) were non-smokers, and 9 (8.57%) were former smokers ($p = 0.000000001$).

Clinicopathological data also revealed significant findings related to the development of lung cancer. Of the patients, 13 (12.38%) were diagnosed with small-cell lung cancer (SCLC), and 92 (87.62%) had non-small-cell lung cancer ($p = 0.000000001$). According to the TNM (Tumor-Node-Metastasis) staging system, 2 cases (2.86%) were in stage I, 23 cases (21.91%) in stage II, 25 cases (22.85%) in stage III, and 55 cases (52.38%) in stage IV ($p = 0.000000001$). Lung cancer grading revealed that 12 (11.43%) were grade I, 48 (45.71%) were grade II, and

Table 1. Demographic and Clinicopathological Features of Lung Cancer Patients

Characteristics	n	Percentages	p-value
Sex:			
Female	34	32.38%	0.0003**
Male	71	67.62%	
Age (years):			
40-49	7	6.67%	
50-59	31	29.52%	
60-69	36	34.29%	0.000001**
70-79	23	21.91%	
80-89	8	7.62%	
Smoking Status			
Smoker	59	56.19%	
Non-smoker	37	35.24%	0.000000001 **
Former smoker	9	8.57%	
Histological Type			
SCLC	13	12.38%	0.000000001**
NSCLC	92	87.62%	
TNM Stage			
Stage I	2	2.86%	0.000000001**
Stage II	23	21.91%	
Stage III	25	22.85%	
Stage IV	55	52.38%	
Histological Grade			
Grade I	12	11.43%	0.000011**
Grade II	48	45.71%	
Grade III	45	42.86%	
Lymph Node Metastases			
Positive	65	61.91%	0.014 *
Negative	40	38.09%	

Data were presented as the number of patients (n), with results also represented as percentages (%). The p (probability) -value was calculated using the Chi-square test, and (*; **) indicates a significant difference between the two groups ($p \leq 0.05$ and $p \leq 0.01$, respectively). Abbreviations: SCLC for Small Cell Lung Cancer; NSCLC for Non-Small Cell Lung Cancer; TNM for a staging system used to assess the size of the tumor (T), the involvement of lymph nodes(N), and the spread of cancer (Metastasis, M)

45 (42.86%) were grade III (p = 0.000011). Additionally, lymph node metastasis was observed in 65 cases (61.91%), compared to 40 cases (38.09%) without metastasis (p = 0.014) (Table 1).

Data were presented as the number of patients (n), with results also represented as percentages (%). The p (probability) -value was calculated using the Chi-square test, and (*; **) indicates a significant difference between the two groups ($p \leq 0.05$ and $p \leq 0.01$, respectively). Abbreviations: SCLC for Small Cell Lung Cancer; NSCLC for Non-Small Cell Lung Cancer; TNM for a staging system used to assess the size of the tumor (T), the involvement of lymph nodes(N), and the spread of cancer (Metastasis, M)

Frequency distribution of -4719A/T (rs2619679) genotype and lung cancer risk

The distribution of *RAD51* -4719A/T genotypes among lung cancer patients was as follows: 13.33% had the AA genotype, 55.24% had AT, and 31.43% had TT. In contrast, all individuals in the control group (100%) exhibited the AA genotype.

The elevated frequencies of the AT and TT genotypes among patients, compared to the AA genotype, differed significantly from those observed in controls ($p \leq 0.01$). Furthermore, a highly significant association was found between the presence of the T allele and increased risk of lung cancer (p = 0.00000001), and the results are shown in Table 2 and Figure 1.

Association between RAD51-4719A/T genotype with demographic and clinicopathological characteristics

The current study found no statistically significant associations ($p > 0.05$) between the *RAD51* -4719A/T SNP genotypes and demographic variables, including sex, age, and smoking status (Table 3). Although these associations were not significant, a higher frequency of the T allele and AT genotype was observed among male lung cancer patients compared to females, patients aged 60–69 years versus other age groups, and smokers compared to non-smokers (p = 0.45, 0.69, and 0.21, respectively).

Similarly, no significant associations were identified between the *RAD51* -4719A/T SNP genotypes and clinicopathological features such as histological subtype, tumor stage, tumor grade, and lymph node metastasis. Nonetheless, the T allele and A/T genotype appeared more frequently among patients with NSCLC than SCLC, those with advanced tumor stage (stage IV), higher tumor grade (grade III), and those with lymph node metastases, although these differences did not reach statistical significance (p = 0.55, 0.3, 0.067, and 0.73, respectively) (Table 3).

Table 2. Distribution of *RAD51* -4719A/T Genotypes and Alleles among Lung Cancer Patients and Healthy Controls

Genotype	Patients (n=105)	Control subjects (n=50)	OR (95% CI)	χ^2	p-value
AA	14 (13.33%)	50 (100%)	1.00 Ref	127.68	
AT	58 (55.24%)	0	NA		0.00000001**
TT	33 (31.43%)	0			
Alleles frequency					
A allele	86 (44.72%)	100(100%)	1.00 Ref	75.67	0.00000001**
T allele	124 (64.48 %)	0	NA		

Data were expressed as number and a percentage (n%). The p (probability) value was calculated using the Chi-square test,, and (**) indicates a significant difference between the two groups ($p \leq 0.01$). Abbreviations: NA, not applicable; n, number; p, probability; OR, odds ratio; 95% Cl, 95%confidence interval.

Table 3. Association of *RAD51*-4719A/T SNP with Demographic and Clinicopathological Characteristics of Lung Cancer Patients

Variables		Genotypes			
	No.	AA (n%)	AT (n%)	TT (n%)	p-value
Sex					
Female	34	3 (8.82%)	18 (52.94%)	13 (38.24%)	0.45
Male	71	11 (15.49%)	40 (56.34%)	20 (28.17%)	
Age					
40-49	7	0	4 (57.14%)	3 (42.86%)	
50-59	31	4 (12.90%)	15 (48.39%)	12 (38.71%)	0.69
60-69	36	7 (19.44%)	20 (55.56%)	9 (25%)	
70-79	23	2 (8.70%)	16 (69.56%)	5 (21.74%)	
80-89	8	1 (12.5%)	4 (50%)	3 (37.5%)	
Smoking Status					
Smoker	59	5 (8.47%)	34 (57.63%)	20 (33.90%)	
Non-smoker	37	8 (21.62%)	17 (45.95%)	12 (32.43%)	0.21
Former smoker	9	1 (11.11%)	7 (77.78%)	1 (11.11%)	
Histological Type					
SCLC	13	1 (7.69%)	9 (69.23%)	3(23.08%)	0.55
NSCLC	92	12(13.04%)	49(53.26%)	31(33.70%)	
TNM Stage					
Stage I	2	0	0	3 (100%)	
Stage II	23	3 (13.05%)	12 (52.17%)	8 (34.78%)	0.3
Stage III	25	3 (12.5%)	14 (58.33%)	7 (29.17%)	
Stage IV	55	7 (12.73%)	33 (60%)	15 (27.27%)	
Histological Grade					
Grade I	12	2 (16.67%)	8 (66.66%)	2 (16.67%)	0.067
Grade II	48	4 (8.34%)	22 (45.83%)	22(45.83%)	
Grade III	45	7 (15.56%)	29 (64.44%)	9 (20%)	
Lymph Node Metastases					
Positive	60	9 (13.84%)	34 (52.31%)	22 (33.85%)	0.73
Negative	45	5 (12.5%)	24(60%)	11 (27.5%)	

Data were presented as the number of patients (n), with results also represented as percentages (%). The p (probability) -value was calculated using the Chi-square test Abbreviations: SCLC, Small Cell Lung Cancer; NSCLC, Non-Small Cell Lung Cancer; TNM, Tumor, Node, Metastases.

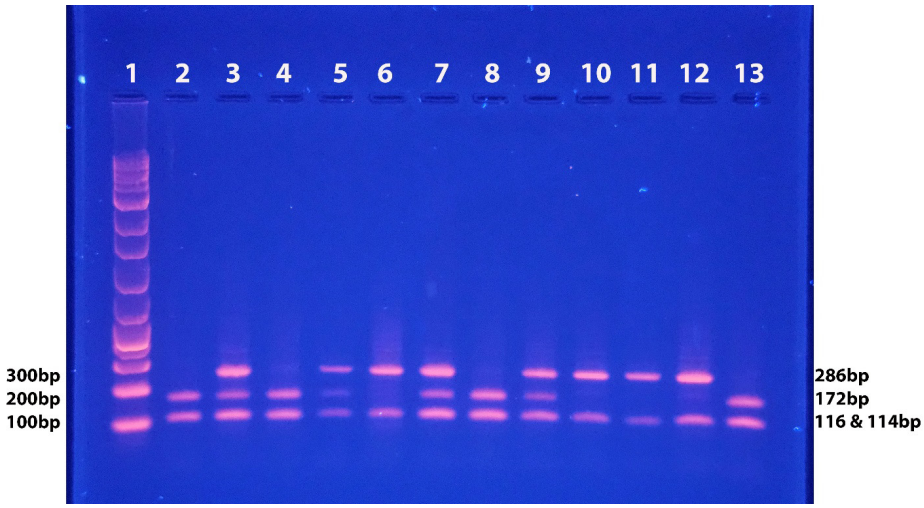

Figure 1. The Electrophoresis Image of PCR -RFLP Analysis of RAD51 -4719 A/T SNP. Lane 1: 100 bp DNA Ladder; Lane 6, 10, 11 and 12: homozygous genotype, AA (286 and 116bp); Lane 3,7 and 9: heterozygous genotype, AT (286, 172, 116, and 114bp); Lane 2, 4, 8 and 13: homozygous genotype, TT (172, 116 and 114bp). Note: The 114 bp and 116 bp fragments co-migrate and appear as a single band due to their similar sizes. Electrophoresis conditions: Agarose gel (1% agarose gel stained with DSRed Nucleic Acid Stain), 60 min, 70 Volt, and 1X TBE buffer.

Discussion

This population-based case-control study was conducted to investigate the association between *RAD51* -4719A/T polymorphisms and the susceptibility to lung cancer within the Iraqi population. *RAD51* protein plays a central role in maintaining genomic integrity through HR repair pathways. Specifically, *RAD51* mediates the critical strand invasion step, which involves the alignment of 3' single-stranded DNA overhangs with a homologous DNA template, thereby facilitating accurate repair of double-strand breaks [14]. Overexpression of *RAD51* has been documented across a range of malignancies, including glioblastoma [15], melanoma [16], breast [17], ovarian [18], pancreatic [19], cervical [20], and non-small cell lung cancer [21].

This aberrant expression is often associated with poor clinical outcomes, largely due to enhanced cellular ability to repair DNA damage induced by chemotherapeutic agents, ultimately contributing to treatment resistance and disease progression [22].

In terms of demographic characteristics, the present study found statistically significant associations between sex, age, and smoking status and the occurrence of lung cancer (Table 1). The data revealed a higher incidence of lung cancer among male patients. Consistently, a study by Al-Hashimi and Alawjar in Iraq reported that 72.44% of lung cancer cases were males, compared to 27.56% females [23]. These findings are consistent with the study by Kratzer et al., which reported that males are more likely than females to develop lung cancer, primarily due to historically higher smoking rates among men [24].

Additionally, the incidence of lung cancer in the current study was highest in the third age group (60–69 years), showing a statistically significant difference ($p = 0.000001$) compared to other age groups. This observation aligns with the results of Torre et al. [25], who suggested that cancer development is closely associated with aging due to physiological processes such as telomere shortening and accumulated DNA damage over time.

Similarly, the findings support those of Chen et al. [26], who examined the relationship between age and clinicopathological characteristics in non-small cell lung cancer patients and found the highest prevalence among individuals aged 65–69 years. This trend is further supported by data from a study conducted in Hong Kong, where approximately 80% of lung cancer cases occurred in individuals aged 60 years and older, indicating that advanced age is a significant risk factor [27].

The current study also found a higher incidence of lung cancer among smokers compared to non-smokers and former smokers. Nicotine, the primary addictive component of tobacco, acts as an agonist to acetylcholine by binding to nicotinic acetylcholine receptors (nAChRs) in the nervous system. This interaction stimulates the release of various neurotransmitters, including gamma-aminobutyric acid (GABA), dopamine, serotonin, norepinephrine, and endorphins [28]. While nicotine itself is not carcinogenic, it contributes to tobacco dependence, alters gene expression, upregulates nAChRs, and has been implicated in the progression of pre-existing lung tumors [29]. Furthermore, numerous studies conducted in Iraq have established a strong link between cigarette smoking and various types of cancers, including breast [30, 31], colorectal carcinoma [32], and oral cancers [33], underscoring the critical role of tobacco exposure in cancer development within the Iraqi population. These findings highlight the pressing need for targeted public health interventions and smoking cessation programs in Iraq to mitigate the burden of smoking-related cancers.

In our study, a statistically significant relationship was observed between lung cancer and various clinicopathological parameters, including histological subtype, tumor stage, tumor grade, and lymph node metastasis. The vast majority of patients were diagnosed with non-small-cell lung cancer, which is consistent with global patterns where NSCLC constitutes the predominant subtype. Most patients were diagnosed with advanced-stage disease (stage IV), with a predominance of moderately to poorly differentiated tumors (grades II and III), and a high proportion of lymph node involvement, reflecting the aggressive nature and late presentation of the disease. These findings may reflect a pattern of delayed cancer diagnosis, which is a common challenge in many low- and middle-income countries (LMICs), including Iraq. Delays in seeking medical attention, limited public awareness of cancer symptoms, and insufficient access to early diagnostic services often result in patients presenting with more advanced disease. A recent WHO report emphasizes that in LMICs, a significant proportion of cancer cases are diagnosed at late stages due to inadequate diagnostic infrastructure and delayed referral pathways (World Health Organization, 2023) [34]. In Iraq specifically, delayed diagnosis is not limited to lung cancer but extends to other diseases as well. For example, diabetes mellitus is frequently detected only after complications arise, leading to high rates of poorly controlled disease [35, 36]. Similarly, microbial and fungal infections are often diagnosed in advanced stages [37-40], complicating treatment and prognosis. Hematologic malignancies such as leukemia [41] are also commonly identified late, further illustrating a broader issue of delayed medical detection across multiple disease types in the Iraqi healthcare context.

These findings were in line with the results reported by Zhang et al., who noted that non-small cell lung cancer was the predominant histological subtype, followed by small cell lung cancer [42]. Similarly, the study by Yang et al. reported that 47.8% of lung cancer patients were diagnosed at stage III or IV, while 46.9% were diagnosed at earlier stages (0, I, or II) [43]. Supporting this, Serin et al. [44] demonstrated that grade III tumors were more prevalent than grade I or II. Other studies have identified grade II tumors as more frequent than grade III in NSCLC cases [45, 46].

Regarding the genetic findings, our study identified a significant association between the *RAD51* -4719A/T (rs2619679) single nucleotide polymorphism and lung cancer. The presence of the T allele was notably higher in lung cancer patients compared to controls, with a higher prevalence of the AT and TT genotypes in the patient group. These results suggest that the T allele may

be linked to an increased likelihood of developing lung cancer. This finding is consistent with previous research indicating that certain genetic variants may influence lung cancer susceptibility. To our knowledge, this is the first study to report such an association in the Iraqi population, suggesting that genetic factors may contribute to lung cancer incidence in this region.

In relation to demographic and clinicopathological parameters, no significant association was observed between sex, age, or smoking status and the *RAD51*-4719A/T genotype in relation to lung cancer risk. However, a higher prevalence of the heterozygous (AT) and mutant homozygous (TT) genotypes was noted in male patients compared to females. Similarly, these genotypes were more commonly observed in older individuals. These patterns suggest that, while no statistically significant correlations were identified, the T allele may still contribute to lung cancer susceptibility within specific subgroups, such as males or elderly patients. Additionally, although not statistically significant, a higher frequency of the T allele and AT/TT genotypes was observed among smokers compared to non-smokers, indicating a possible trend that warrants further investigation in larger cohorts.

The *RAD51* gene, involved in DNA repair through homologous recombination, plays a crucial role in maintaining genomic integrity. Sex-based differences in DNA repair efficiency may contribute to variations in cancer susceptibility, with males potentially at a higher risk due to their genetic profile [47]. Additionally, the study by Sedelnikova et al. highlighted the decline in DNA repair efficiency with age, making older individuals more susceptible to accumulating genetic mutations linked to cancer [48]. Furthermore, cigarette smoke, which contains various harmful chemicals, has been shown to directly damage DNA or produce reactive oxygen species, contributing to oxidative stress and further DNA damage [49].

No statistically significant variations ($p > 0.05$) were observed in the distribution of *RAD51*-4719A/T SNP genotypes with respect to histological subtype, tumor stage, grade, and lymph node metastasis. However, the highest frequency of the mutant T allele (in both AT and TT genotypes) was detected in patients with NSCLC, advanced tumor stages (stage III-IV), grade II tumors, and positive lymph node metastasis. These findings align with those of Xu et al. [50], who reported significantly higher *RAD51* expression in stage IV tumors compared to stage I and stage II tumors, as well as in bone marrow metastases in neuroblastoma. Similarly, Romanowicz et al. [51] did not find an association between *RAD51*-4719A/T polymorphisms and cancer progression as assessed by tumor size and node status.

Single nucleotide polymorphisms are a major source of genetic variation, and their presence in the promoter region of the *RAD51* gene can influence its expression, modifying the efficiency of the efficiency of homologous recombination [13]. Hasselbach et al. reported that two distinct SNPs located upstream of the first exon of the *RAD51* gene can significantly impact promoter-driven-expression in vitro. These promoter-region polymorphisms, situated adjacent to exon 1, appear to reduce the repressing function exerted by the downstream region beyond base pair -58, resulting in a marked increase in promoter activity [52]. Additionally, findings by Li et al. indicated that *RAD51* expression is positively correlated with tumor differentiation. Elevated *RAD51* levels were notably associated with the presence of lymphatic metastasis and an increased rate of tumor relapse [53].

The lack of significant differences observed in this study could be attributed to the relatively small sample size. Consequently, further investigations with a larger sample size are needed to validate these findings.

In conclusion, this study provides the first evidence of an association between the *RAD51* -4719A/T (rs2619679) polymorphism and lung cancer in an Iraqi population. The presence of the T allele particularly in AT and TT genotypes was significantly more common among lung cancer patients than in healthy controls, suggesting a potential role for this genetic variant in lung cancer susceptibility. While no significant associations were observed between *RAD51* genotypes and demographic or clinicopathological variables such as sex, age, smoking status, tumor histology, stage, grade, or lymph node metastasis, the T allele was more frequently found in males, older, smoking patients, as well as those with NSCLC, advanced-stage disease, and positive nodal involvement. These trends, though not statistically significant, may reflect underlying biological mechanisms linked to *RAD51* function in DNA repair and cancer development. Limitations such as the small sample size may have impacted the statistical power to detect additional associations. Therefore, future studies with larger cohorts and functional analyses are needed to confirm these findings and further elucidate the role of *RAD51* in lung carcinogenesis.

Author Contribution Statement

RMA: Conceptualization, methodology, and original draft preparation supervision. ZMJ: Literature review, methodology, writing and editing. All authors have read and approved the final version of the manuscript.

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Approval

This work has not been approved by any scientific or professional body.

Ethical Statement

Ethical approval was obtained through institutional agreement at the authors' affiliated university; all procedures followed the institution's ethical guidelines for research involving laboratory work.

Conflict of Interest

Authors declare no conflicts of interests related to this study.

Availability of data

The data generated and analysed during this study are available from the corresponding author upon reasonable request.

Study Registration

The study is not registered in any registering dataset.

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