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Investigation of CA15-3 and IgE in Iraqi lung cancer patients: A biochemical and immunological analysis

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Abstract

Introduction: Lung cancer (LC) is one of the leading causes of cancer death worldwide. A number of single nucleotide polymorphisms are associated with the risk of LC, which deserves to be studied further. Aim: The purpose of this study was to identify immunological and biochemical markers for Iraqi lung cancer patients. Method: Fifty LC Iraqi patients and 50 apparently healthy people, who composed the control group, were involved in the study. Blood samples were used for biochemical and immunological studies. DNA extraction and polymorphism of the EXO1 and CHRNA5 genes were carried out via polymerase chain reaction. Results: Lactate dehydrogenase (LDH), blood urea, and serum creatinine levels were significantly greater ($P \leq 0.01$) in LC patients compared with control.

In contrast, adenosine deaminase (ADA), HbA1c, and Hb were significantly decreased. Moreover, the levels of immunoglobulin-E (IgE) and cancer antigen 15–3 (Ca-153-) are increased in LC patients. Scanning the EXO1 gene revealed that the percentage of the mutant homozygous (AA) and (GA) genotypes is greater than that of the wild-type homozygous (GG) genotypes. Homozygous (GG) was highly significant in the control group than other genotypes (AA and GA). Conversely, the CHRNA5 gene revealed that, in comparison with other genotypes (GA, GG), the AA genotype was considerably greater in LC patients. However, the number of homozygous GG genotypes was more significant in the control group than in other groups. EXO1 and CHRNA5 were significantly higher in all the biochemical markers associated with the mutant (AA) genotype. While they were significantly normal in the GG genotype, they also decreased in ADA, HbA1c, and Hgb. IgE was significantly increased in all genotypes. Conclusions: The results of the present study clarify that promoting a precise estimate of the clinical utility of two significant biomarkers, CA153- and IgE, may be helpful in lung cancer surveillance. Therefore, this study highlights the warning of lung cancer patients.

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Introduction

Uncontrolled cell development in lung tissues is a hallmark of lung cancer, a malignant tumor of the lung [1]. This growth has the potential to metastasize or spread outside of the lung into surrounding tissue or other body regions if treatment is not received. Small-cell lung carcinoma (SCLC) and non-small cell lung carcinoma (NSCLC) are the two primary forms of lung cancer [2, 3]. Certain alterations in the DNA of lung cells can be caused by several risk factors for lung cancer [4]. These alterations may result in aberrant cell proliferation [5]. Genomic instability and mutations caused by DNA damage result in malignant transformation [6,7]. Since ADA is a purine-based chemical product that includes sugar molecule ribose, it is crucial to the process of cell differentiation[8]. Severe combined immunodeficiency disease is caused by an ADA deficit [9,10]. This is mostly due to the release of ectopic hormones from tumor cells, which are present at high concentrations in the blood of individuals suffering from lung, colorectal, and liver cancer, among other malignant tumors[11]. HbA1c, or glycated hemoglobin, is linked to an increased risk of several malignancies, including lung cancer [12,13]. This study aimed to determine the possible role of tumor markers such as CA153- in the serum of patients diagnosed with lung cancer.

On the other hand, the chronic inflammation theory postulates that allergies increase the risk of cancer in affected organs due to tissue remodeling and inflammation-induced DNA damage [14].This study aimed to evaluate the relationships between biochemical and hematological parameters and their relationships with the genotypes of the CHRNA5 and EXO1 genes in lung cancer patients and the degree of polymorphism variance, which can provide a clear picture of the early detection of lung cancer.

Materials and Methods:

The current study included 100 participants divided into two groups: 50 patients and 50 controls.

Blood Sampling

Four milliliters of venous blood samples were withdrawn from all the subjects. Each blood sample was divided into two equal parts; the first was used to separate the serum for biochemical and immunological tests, while the rest of the blood was used for DNA extraction. The serum was stored at -20°C. The patient group comprised 50 pretreated Iraqi lung cancer patients diagnosed by specialists at both Al-Kadhimiya Teaching Hospital and the Medical Oncology Hospital of the Medical City in Baghdad on the basis of medical signs and symptoms in addition to the results of X-ray examination, computed tomography (CT), biochemical tests, and biopsy results for the period from the 1st of November 2022 to the end of March 2023.

Control Group

Fifty apparently healthy individuals without a family history of lung cancer or any other type of cancer matched by age and sex were included in the present study.

Biochemical tests

Lactate dehydrogenase (LDH) and adenosine deaminase (ADA) were estimated by fully automated clinical chemistry analyzer, using serum creatinine, blood, and urine levels, measured with an automated biochemistry analyzer (Promega, USA)

The normal values for these biochemical tests were as follows:

ADA: 35–160 U/L, LDH: 140–280 U/L, Urea: 15–45 mg/dl Creatinine: < 1 mg/dl

Immunological tests

Cancer antigen 15–3 (Ca-153-) and immunoglobulin E (IgE) were estimated by using an IMMULITE device, which is a chemiluminescent immunoassay system with a throughput of 120 tests/hour.

Ca. 153- cutoff.

Hematological tests

Hemoglobin was measured in all the subjects via a SAMSUNG automatic hematology analyzer according to the manufacturer's instructions. The normal range for hemoglobin is 12.0 to 17.0 grams per deciliter.

Hemoglobin-A1c

A fully automated assay called the CLOVER A1cTM self system was used to calculate the percentage of hemoglobin A1c (HbA1c%) in whole blood. The test cartridge is composed of a cartridge and a bag of reagents that have all the ingredients needed to measure hemoglobin A1c. HbA1c has a normal range of 4–6%.

Principle of Biochemical and Immunological Analysis

All biochemical and immunological tests were fully automated via the CLOVER A1cTM self-system and IMMULITE devices. We followed the manufacturer's instructions to determine biochemical and immunological parameters via kits supplied by immune laboratory ELITech Group, France.

DNA Extraction

DNA extraction was conducted with the Genomic DNA Extraction Kit in accordance with the manufacturer's instructions (Themo fisher Scientific-USA).

Estimation of the DNA concentration and purity

The DNA concentration and purity were measured via a (Themo fisher Scientific-USA).

One microliter of each DNA sample was loaded onto the lens of the nanodrop, and the result appeared on the laptop screen attached to the nanodrop. The lenses were subsequently cleaned with distilled water after each sample, and the other samples were subsequently measured. The purity was detected by determining the ratio of the optical density (OD) at 260280/ nm to detect contamination of the samples with protein.

Agarose Gel Electrophoresis

After DNA extraction, agarose gel electrophoresis was performed to determine the presence and integrity of the extracted DNA [15,16].

Detection of the rs1047840 and rs16969968 SNPs

Preparation of primers and probes

Real-time polymerase chain reaction (RT–PCR) was performed by using specific primers and probes. Alpha DNA Company supplied the primers and probes as lyophilized products of different picomole concentrations. In accordance with the manufacturer's instructions, the primers and probes were dissolved in free nuclease water to obtain a final concentration of 100 pmol/µl, which was used as a stock solution; 10 µl of this mixture was added to 90 µl of free nuclease water to obtain 10 pmol/µl of primer and probe

solutions at the final concentration utilized in the PCR technique.

Genotyping Allelic Discrimination via Quantitative Real-Time Polymerase Chain Reaction

Genotyping – Allelic discrimination of rs1047840 and rs16969968 was performed via quantitative real-time PCR (qRT–PCR) with specific primers and probes.

Statistical analysis

The SAS (2012) program was used to determine how different factors affect the study parameters. The least significant difference (LSD) test (analysis of variation, ANOVA) or the t test was used to compare means significantly. To compare percentages (0.05 and 0.01 probability), the chi-square test was used. The odds ratio (OR) and CI were estimated in this study.

Results

Biochemical and immunological analysis:

Biochemical and immunological tests were performed for 50 LC patients and fifty healthy controls in this study. All tests were conducted via modern and advanced equipment. Comparisons of ADA, LDH, and Bl. Urea, S, and creatinine are presented in Table 1.

Table 1: Comparisons of ADA, LDH, and Bl. Urea and S. Creatinine

Group	Mean ± SE			
	ADA 35 - 160 (U/L)	LDH 140 - 280 (U/L)	Urea 15 – 45 (mg/dl)	Creatinine < 1 (mg/d)
Patients	32.08 ± 0.85	292.36 ± 5.88	48.50 ± 1.09	1.190 ± 0.08
Control	77.60 ± 5.00	210.66 ± 5.16	35.76 ± 1.01	0.630 ± 0.03
T test	10.069 **	15.543 **	2.952 **	0.177 **
P value	0.0001	0.0001	0.0001	0.0001
.(P≤0.01) **				

ADA: Adenosine deaminase, LDH: Lactate dehydrogenase.

Comparisons between the LC patient group and apparently healthy control group and Hgb are presented in Table 2.

Table 2: Comparison of HbA1c, Hgb and WBC levels between the lung cancer patient group and the control group.

Group	Mean ± SE	
	HbA1c 4 – 6%	Hgb 12 – 16 g%
Patients	3.78 ± 0.11	11.86 ± 0.35
Control	4.68 ± 0.08	13.75 ± 0.17
T test	0.282 **	0.781 **
P value	0.0001	0.0001
.(P≤0.01) **		

HbA1c: hemoglobin-A1c, Hb: hemoglobin.

The results in Table 3 show that IgE was positive (82%) in the patients in the LC group, whereas it was positive in the controls (4%).

Table 3: Comparison of IgE levels between the lung cancer patient group and the control group.

Results	Patients No. (%)	Control No. (%)	P value
Positive (+ve)	41 (82.00%)	2 (4.00%)	0.0237 *
Negative (-ve)	9 (18.00%)	48 (96.00%)	0.0237 *
P value	0.0001 **	0.0001 **	---
(P≤0.05)**, (P≤0.01) *			

IgE: Immunoglobulin E

The results in Table 4 show that CA153- was high (84%) among the patients in the LC group.

Table 4: Distribution of CA15-3 in patients with lung cancer.

Results of CA 15-3	No.	(%)
abnormal	42	84%
Normal	8	16%
Total	50	100%

CA 15-3: Cancer Antigen 15-3

Molecular Study

Genomic DNA Extraction

The results of the DNA extraction experiment gave a good yield of the extracted DNA (pure, sharp DNA band), as shown in Figure (1). The extracted DNA was quantified via a NanoDrop spectrophotometer. The concentration of the DNA samples was 95 ng/µl, which is within the agreeable range of 80–120 ng/µl. The purity range was approximately 1.9, which is compatible with the accepted 260280/ ratio for pure DNA, which is between 1.7 and 1.9.

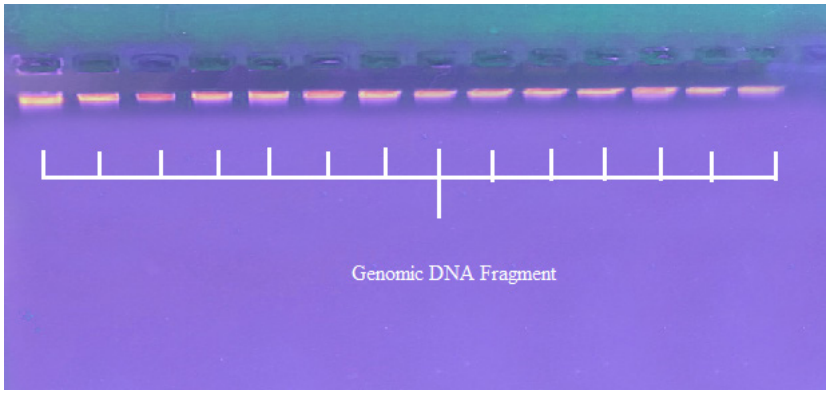
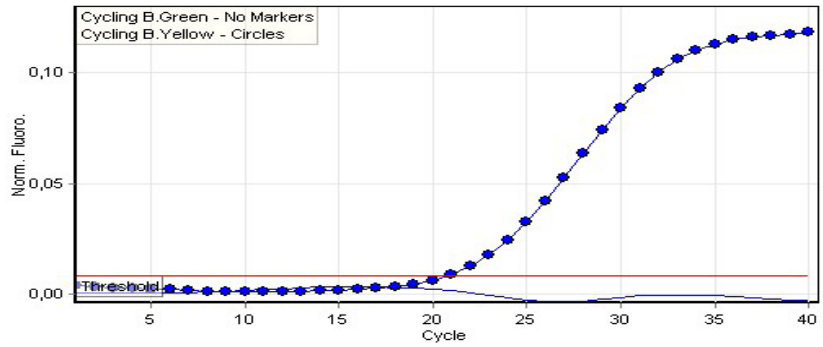


Figure (1): Gel electrophoresis of genomic DNA visualized under UV after staining with ethidium bromide on a 1% agarose gel at 70 volts for 30 minutes.

Polymorphisms of the EXO1 and CHRNA5 Genes

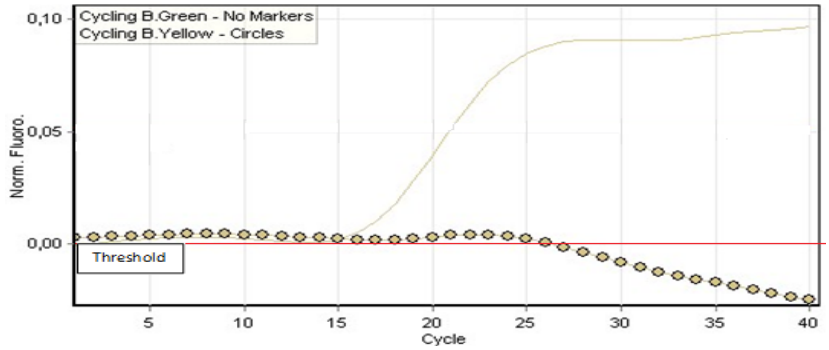
Genotype and allele frequency distributions

The following figures (2, 3, 4) show the results of real-time PCR.



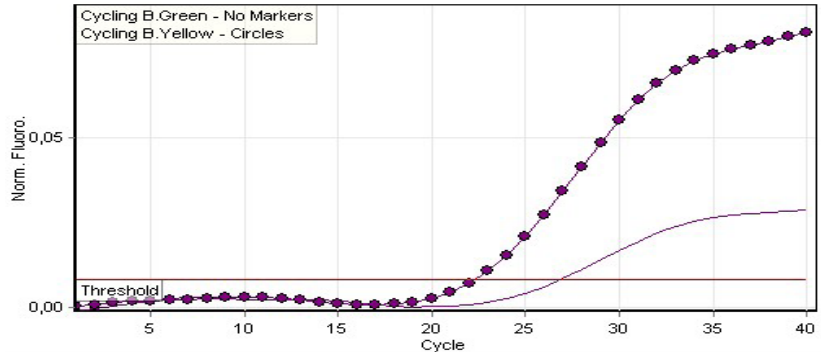
Color	Name Genotype	Cycling B. Green	Cycling B. Yellow
	Mutant	No Reaction	Reaction

Figure (2):
Homozygous AA genotype; only the VIC-BHQ probe was hybridized with the DNA samples.



Color	Name Genotype	Cycling B. Green	Cycling B. Yellow
	Wild Type	Reaction	No Reaction

Figure (3):
Homozygous GG genotype; only the Fam-BHQ probe is hybridized with DNA samples.



Color	Name Genotype	Cycling B. Green	Cycling B. Yellow
	Heterozygous	Reaction	Reaction

Figure (4):
Heterozygous GA genotype, with both the VIC and the fam probe hybridized with DNA samples.

EXO1 gene (rs1047840) G>A polymorphism

Table (5) shows the distribution of genotypes and allelic frequency of EXO1gene polymorphism (rs1047840) in LC patients and the apparently healthy control group.

In the LC patient group, the mutant homozygous (AA) genotype (62%), followed by the mutant heterozygous (GA) genotype (32%), was highly significantly elevated (p<0.01) compared with the wild-type homozygous (GG) genotype O.R.=1.46, indicating that this genotype represents a risk factor for the occurrence of LC. Compared with those of the other genotypes (AA and GA), the percentage of the homozygous (GG) genotype (84.00%) significantly increased (p<0.01) in the control group, with an OR of 1.683, indicating that this genotype was a protective factor against LC. The frequencies of the G and A alleles were 0.22 and 0.078, respectively, in the patient group and 0.91 and 0.09, respectively, in the health control group. This finding indicated that A was a risk allele of LC, whereas the G allele was a protective allele against LC.

Table (5): Distribution of the rs1047840 genotype and allele frequency in LC patients and the control group.

Genotype rs1047840	Patients (50) No. (%)	Control (50) No. (%)	Chi-square	O.R. (C.I.)
GG	3 (6.00%)	0.0001 ** 42 (84.00%)		1.683 (0.97-1.82)
GA	16 (32.00%)	7 (14.00%)	0.0078 **	1.45 (0.82-1.66)
AA	31 (62.00%)	1 (2.00%)	0.0001 **	1.462 (0.91-1.73)
Allele frequency				
G	0.22	0.91	--	--
A	0.78	0.09	--	--
(P≤0.01) **				

CHRNA5 gene (rs16969968) G>A polymorphism

Table (6) shows the distribution of genotypes and allelic frequency of CHRNA5gene polymorphism (rs16969968) in LC patients and an apparently healthy control group.

The prevalence of the mutant homozygous (AA) genotype (74.00%) was significantly greater in the LC patient group (p<0.01) than in the other genotypes, with O.R.= 1.702, indicating that this genotype represents a risk factor for the occurrence of LC. The homozygous (GG) genotype (76.00%) was more significant (p<0.01) in the control group than the other genotypes, with OR = 1.783, indicating that this genotype is a protective factor against LC. The frequencies of the G and A alleles confirmed that they were 0.83 and 0.17, respectively, in apparently healthy subjects, whereas they were 0.17 and 0.83, respectively, in LC patients. This finding indicates that A is a risk allele of LC, whereas G is a protective allele against LC.

Table (6): Distribution of the rs16969968 genotype and allele frequency in lung cancer patients and controls

Genotype rs16969968	Patients (50) No. (%)	Control (50) No. (%)	Chi-square	O.R. (C.I.)
GG	4 (8.00%)	38 (76.00%)	0.0001 **	1.783 (0.91-1.88)
GA	9 (18.00%)	7 (14.00%)	0.1274 NS	0.372(0.19-0.62)
AA	37 (74.00%)	5 (10.00%)	0.0001 **	1.702(0.87-1.86)
Allele frequency				
G	0.17	0.83	--	--
A	0.83	0.17		
(P≤0.01) **				

Relationships between EXO1 gene genotypes and results of biochemical and immunological analyses

According to the results presented in Table (7), LDH, blood urea, and serum creatinine (312.48 ±5.57; 53.410.94± a; and 1.362 ±0.11, respectively) were significantly higher (P≤0.01) in LC patients with the mutant homozygous (AA) genotype. However, 220.33 ±19.6, 35.33 ±0.33, and 0.833 ±0.03, respectively, were significantly (P≤0.01) normal in the protective wild-type homozygous (GG) genotype. These results indicate that these markers are associated with the risk of the AA genotype in LC patients in the present study.

Table 7: Relationships between Genotype *EXO1* (rs1047840) and LDH, blood urea and serum creatinine in lung cancer patients.

Genotype (rs1047840)	LDH 140 - 280 (U/L) mean±SD	Urea 15 – 45 (mg/dl) mean±SD	Creatinine < 1(mg/d) mean±SD
GG (3)	220.33 ±19.6 c	35.33 ±0.33 c	0.833 ±0.03 c
GA (16)	274.06 ±6.15 b	42.00 ±0.84 b	1.043 ±0.09 b
AA (31)	312.48 ±5.57 a	53.41 ±0.94 a	1.362 ±0.11 a
LSD value	7.008 **	4.972 **	0.607 **
(P≤0.01) **			

Table 8: Relationships between Genotype EXO1 (rs1047840) and ADA, HbA1c and Hgb in lung cancer patients.

Genotype (rs1047840)	ADA 35 - 160 (U/L)	HbA1C 4 – 6%	Hgb 12 - 16 g%
GG (3)	45.00 ±1.52 a	5.67 ±0.33 a	12.67 ±0.33 a
GA (16)	36.62 ±0.78 b	5.56 ±0.15 a	11.50 ±0.16 b
AA (31)	28.45 ±0965 c	4.42 ±0.10 b	9.96 ±017 c
LSD value	3.694 **	0.630 **	0.909 **
(P≤0.01)			

The results of the IgE results in Table 9 show a significant (P≤0.01) increase in IgE (96.77%) in the risk genotype (AA) LC patients compared with the protective wild homozygous (GG) genotype, indicating that IgE was associated with the risk of LC.

Table 9: Relationships between Genotype EXO1 (rs1047840) and IgE in lung cancer patients.

Genotype (rs1047840)	IgE	
	Positive (41)	Negative (9)
GG (3)	1 (33.33%)	2 (66.67%)
GA (16)	10 (62.50%)	6 (37.50%)
AA (31)	30 (96.77%)	1 (3.23%)
Chi-Square	14.053 **	14.053 **
(P≤0.01) **		

Relationships between the CHRNA5 genotype and biochemical and immunological analyses

According to the results presented in Table (10), LDH, blood urea, and serum creatinine (315.20±0.93 53.13 ;6.57± a; and 1.344 ±0.12, respectively) levels are considerably greater (P≤0.01) in patients with the mutant homozygous (AA) genotype. The values of 232.33 ±27.29, 35.33 ±0.33, and 0.833 ±0.03, respectively, were significantly (P≤0.01) normal in the protective wild-type homozygous (GG) genotype. These results indicate the risk of the (AA) genotype in LC patients within the present study.

Table 10: Relationships between the *CHRNA5 genotype* (rs16969968) and LDH, blood urea and serum creatinine in lung cancer patients.

Genotype (rs16969968)	LDH 140 - 280 (U/L)	Urea 15 – 45 (mg/dl)	Creatinine < 1(mg/d)
GG (4)	232.33 ±27.29 a	35.33 ±0.33 c	0.833 ±0.03 a
GA (9)	272.87 ±7.87 b	42.00 ±0.84 b	0.937 ±0.02 b
AA (37)	315.20 ±6.57 c	53.13 ±0.93 a	1.344 ±0.12 c
LSD value	37.867 **	4.841 **	0.598 **
(P≤0.01) **			

Table (11) indicates that although the mutant homozygous (AA) genotype was a risk genotype for LC in this study, ADA, HbA1C, and Hgb decreased highly significantly (p<0.01) (29.00 ±0.65; 4.36 ±0.08; 10.03 ±0.15, respectively) in LC patients with this genotype compared with those with the wild-type homozygous (GG) genotype, indicating that these markers decrease with the risk of LC.

Table 11: Relationships between Genotype CHRNA5 (rs16969969) and ADA, HbA1c and Hgb in lung cancer patients.

Genotype (rs16969968)	ADA 35 - 160 (U/L)	HbA1C 4 – 6%	Hgb 12 - 16 g%
GG (4)	45.00 ±1.52 a	5.67 ±0.33 a	12.33 ±0.33 a
GA (9)	35.50 ±1.28 b	5.43 ±0.18 a	11.62 ±0.15 a
AA (37)	29.00 ±0.65 c	4.36 ±0.08 b	10.03 ±0.15 b
LSD value	4.456 **	0.626 *	0.831 *
(P≤0.05) *			

Table 12 shows a noteworthy (P≤0.01) increase in IgE (89.19%) in the risk genotype (AA) LC patients compared with that in the protective wild-type (GG) genotype patients, indicating that IgE was associated with the risk of LC.

Table 12: Relationships between the CHRNA5 genotype (rs16969968) and IgE in lung cancer patients.

Genotype	IgE	
(rs16969968)	Positive (+ve) (41)	Negative (-ve) (9)
GG (4)	1 (25.00%)	3 (75.00%)
GA (9)	7 (77.78%)	2 (22.22%)
AA (37)	33 (89.19%)	4 (10.81%)
Chi-Square	12.783 **	12.783 **
(P≤0.01) **		

Discussion

The ADA results (means ± SE) in Tables 4--6 are highly significantly different ($p<0.01$), as the ADA level was lower in the patient group (32.08 ± 0.85) than in the control group (77.60 ± 5.00). These results agree with those of previous studies [17,18]. Another study reported that the mean serum ADA level in the LC group was lower than the mean serum ADA level in the other groups [19,20]. Additionally, a previous study proposed that the mean levels of ADA were significantly higher for tuberculous patients than in LC patients. It is recommended that initial ADA screening be used in conjunction for differential diagnosis between tuberculous pleurisy and LC. Another study comparing LDH levels between patient and control groups revealed a highly significant increase ($p<0.01$), as the mean ± SE of LDH was greater in the patient group (292.36 ± 5.88) than in the control group (210.66 ± 5.16) [21] and [22]. The results of the comparison between the patient group and the control group in terms of blood urea content were highly significantly ($p<0.01$) greater in the patient group (48.50 ± 1.09) than in the control group (35.76 ± 1.01), and these results agree with those of previous studies [23,24].

Some studies have shown that patients who have a high increase in blood urea have a 13-fold increased risk of early death. The results revealed a noticeable increase in the high level of urea in the blood of patients with LC due to physiological changes that lead to hormonal and enzymatic changes that affect the body system and the urinary system, and this result was compatible with that of [25,26,27]. Progressive renal breakdown from lung metastases occurs first and foremost by parenchymal distortion in addition to tubular destruction through tumor cells. However, obstruction from sloughed parenchyma or tumors, vascular invasion in addition to injury with thrombosis, or lymphatic obstruction are possible[28,29,30].

The results of the comparison between the patient group and the control group with respect to HbA1c indicated highly significant differences ($p<0.01$), as the mean ± SE was lower in the patient group (3.78 ± 0.11) than in the control group (4.68 ± 0.08) (Table 2).

Hemoglobin-A1C (HbA1c) is linked with increased risk of cancers, such as LC, and it is a significant predictive factor for the development of LC. Patients who have HbA1c >6.15% should be treated with greater caution. HbA1c is associated with cancer incidence and/or cancer mortality[31,32,33]. The decrease in HbA1c, according to the results of the present study, may be because the majority of patients suffer from weight loss, which leads to a decrease in the value of HbA1C, or perhaps because lung cancer does not metastasize to the pancreas, as most LC patients are in the first stage of LC[34].

Compared with that in the control group, the percentage of IgE in the LC patient group was significantly greater in the present study. Previous studies have suggested that there may be a connection between allergies and cancer that has long been hypothesized, but despite substantial investigations, no clear correlation has been found [35]. Since the lung is an organ that is in close contact with the environment, allergens and carcinogens can easily affect it. The predominant state of inflammation in this area promotes the progression of cancer, making immune surveillance secondary. In addition to the association between lung cancer and asthma, atopic dermatitis and skin cancer are related. Atopic dermatitis causes large, irritated patches of skin that serve as a gateway for carcinogens and the required microenvironment [36,37].

Smoking control is crucial when risk factors for lung cancer development are examined because tobacco is clearly the primary carcinogen that causes lung tumors [38]. Another study demonstrated a positive association between a history of asthma and Licit, increasing the risk for both nonsmoking men and nonsmoking women [39]. A Taiwanese study revealed that smoking and asthma increase the risk of LC. RITTMEYER et al. reported that a connection between allergies and cancer has been suspected for a long time, but despite extensive research, no definite association has been determined [40]. Regarding cancer in general, no clear relationship, either positive or negative, with allergies can be experiential.

On the other hand, asthma was found to be a risk factor for the emergence of LC. A positive correlation can be explained by the fact that allergies are accompanied by inflammatory reactions that create an ideal environment for carcinogenesis. These types of inflammation affect only certain regions; however, they have systemic consequences that improve immune surveillance and prevent cancer [41].

Dalam et al. reported that CA153- is a useful marker in patients with a confirmed diagnosis of LC. CA153- is interrelated with the primary tissue and metastasis of lung adenocarcinoma (LAC) [42].

Lung squamous cell carcinoma (LSCC) metastases are linked to CA125 levels and primary tissue [43]. There was a correlation between the CA153- level and the lung adenocarcinoma (LAC) T, N, and M stages. In addition to being correlated with lung squamous cell carcinoma (LSCC), CA153- may also be associated with metastasis from original tissue, lymph nodes, and distant sites. In LSCC, CA153- can be a sign of distant metastases [44, 45].

Previous studies reported that high levels of CA153- in pleural effusions are associated with high suspicions of malignant effusions and CA153-, which apparently has high specificity for LC and low sensitivity and high specificity. Finally, CA 153-, an important indicator of the occurrence of LC, increases in level due to the high level of cancer due to the growth and spread of these cells, which is an approved indicator for the diagnosis of cancer, particularly LC [46,47,48].

The results in the table show that ADA, HbA1C, and Hgb were highly significantly decreased ($p<0.01$) (28.45;0965± ±017 9.96 ;±0.10 4.42, respectively) in LC patients with the mutant homozygous (AA) genotype, although it was a risk genotype for LC within the present study rather than in LC patients with the wild-type homozygous (GG) genotype, indicating that these markers decrease with the risk of LC.[49] reported that pretreatment HbA1c levels are a significant prognostic factor for locoregional recurrence-free survival in patients with stage III non-small cell lung cancer treated with radical radiotherapy. Routine monitoring of pretreatment HbA1c levels and aggressive glycemic control may be considered to prevent the development of locoregional recurrence in these patients. Additionally, Hua et al. reported that prediabetes and T2D are associated with an increased

incidence of lung cancer. The increased risk of incident lung cancer is more pronounced across HbA1c values of 32–42 mmol/mol, which are currently considered normal values [50].

The result of EXO1 gene polymorphism refers to the relationship between the frequency of this SNP and LC. The EXO1 (rs1047840) polymorphism may be a genetic susceptibility marker for LC [51]. reported that there was a significant association between the EXO1 (rs1047840) polymorphism and LC and that the (AA) genotype was the risk genotype [52]. investigated the effects of rs1047840 genotypes and alleles on LC occurrence and reported a significantly increased risk of LC among Taiwanese subjects. Additionally, the CHRNA5 gene polymorphism results agreed with those of [53].who demonstrated that the A allele was associated with a high risk of LC.

Conclusions

The results of the present study clarify that promoting a precise estimate of the clinical utility of two significant biomarkers, CA153- and IgE, may be helpful in lung cancer surveillance. Therefore, this study highlights the warning of lung cancer patients.

Ethical approval

This study was conducted in accordance with the ethical standards stipulated in the Declaration of Helsinki. Before the samples were collected, written and verbal consent was obtained from the patients after review and approval of the study protocol, and the subject›s information was provided by the local ethics committee according to document number 1385 dated of 92022/3/ to obtain this approval.

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Conflict of interest

The authors declare that there are no conflicts of interest in the publication of this manuscript.

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Data availability:

All data were ready any time if requested.

Author Contribution Statement:

Omer Salim Ghalib; Ashjan Mohammed Hussein; Maeda Hussain Mohammad; Alyaa Jabbar Qasim; and Wiaam Ahmed AL-Amili performed the experimental tests. Alyaa Jabbar Qasim; Omer Salim Ghalib; Maeda Hussain Mohammad; and Ashjan Mohammed Hussein; performed the results analysis. Omer Salim Ghalib; Maeda Hussain Mohammad; Ashjan Mohammed Hussein; wrote the article.

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