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A Chemokine CXCL14 and Its Relationship to Biomarkers for Both Small and Non-Small Cell Carcinomas

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ABSTRACT

Worldwide, lung cancer is still the biggest killer when it comes to cancer, arising from uncontrolled cell division in lung tissues. A homeostatic chemokine with a high degree of conservation, CXCL14 is expressed in epidermal epithelia, playing a key role in immune cell maturation and epithelial regulation. It is the only chemokine known to localize within the tumor microenvironment, contributing to immune surveillance. This study aims to evaluate CXCL14 as a possible of biomarker a prediction of lung cancer outcomes. The materials and methods are a case-control study conducted on 180 participants (aged 45–77): There were 36 cases of "SCLC is a kind of LC", 54 cases of "LC of (NSCLC)", and 90 were healthy controls. CXCL14 levels were measured using ELISA, along with CBC, cholesterol, triglycerides, and liver enzymes (ALT, AST, ALP). Statistical analysis assessed correlations between CXCL14 and (LC) progression. The findings for a study demonstrated that CXCL-14 levels are seen to a significantly lower in stage III compared to stage IV in both NSCLC and SCLC, with a more pronounced decline in NSCLC at stage IV. Linear regression showed a positive correlation between CXCL14 and cholesterol, triglycerides, NLR, ALT, AST, and ALP, while a negative correlation was observed with hemoglobin (Hb) and HDL. CXCL14 demonstrated high diagnostic accuracy, with cut-off values of 120.007 pg/mL for SCLC (AUC = 0.846, p = 0.000) and 87.054 pg/mL for NSCLC (AUC is 0.832, p is 0.000). Conclusions, these findings offer that CXCL14 is a promising biomarker for lung cancer diagnosis and monitoring. Its involvement in lung cancer cell motility also highlights its potential role in predicting metastasis, making it a valuable tool for early detection and prognosis.

Keywords: *small cell carcinoma (SCLC), lung cancer(LC),* **,** *, CXCL14, non-small cell carcinoma (NSCLC)*

1. INTRODUCTION

The primary issue of global cancer mortality and prevalence is carcinoma of the lungs which has led to two million diagnoses and 1.8 million fatalities. The rising incidence of (LC) worldwide is mostly responsible for the increasing use of tobacco products and the industrialization of emerging nations' rise[1]. Radon, resulting from the natural decay of subterranean uranium, is lung cancer's secondary leading cause in affluent nations[2]. All environmental exposures, including air pollution, arsenic, and HIV and TB infection, as well as occupational hazards like asbestos, have been linked to lung carcinogenesis[3]. Simultaneously, it has been postulated that the risk of developing COVID-19, electronic cigarettes, heated tobacco products, and cannabis consumption is elevated[1]. Iraqi Cancer Register reported the annual report, which introduced the total number of new cancer cases during 2022 which was 39.068 lung cancer is the 3rd most common cancers in Iraq and In the initial report on cancer in males, there were 2,853 cases of lung cancer (872 in females and 1,981 in males), while in 2023, the total rose to 43,062, with lung cancer accounting for 3,020 cases (981 females and 2,129 males). The predominant histologic classifications of "small cell lung cancer (SCLC; 13%) and lung cancer are non-small cell lung cancer (NSCLC; 84%)", which inform therapeutic strategies[5]**.**

By screening at-risk populations, diseases may be caught early, when they are more easily treated or even cured[6]**.** According to a study published in Japan Radiographic Screening and Diagnosis, The mortality rate from lung cancer was reduced by 25% for individuals who underwent annual chest X-ray screenings at health clinics[7]. Bronchoscopy is the leading diagnostic technique for establishing a definitive histological diagnosis of lung cancer. Additionally, sputum cytological analysis, especially when multiple samples are examined, serves as another valuable method for detecting

Elevated leukocyte levels are often thought to result from bacterial infections, especially when granulocytes are the most numerous. However, it is important to consider additional factors, including advanced cancer, bleeding, and the use of corticosteroids.[9]**.** Fever serves as a distinguishing characteristic that is more frequently observed in individuals with infections. In fact, a notable correlation exists between the likelihood of lung cancer and various circulating inflammatory and immunological markers.[10].The researchers found evidence for a positive relation between count of white blood cell and lung cancer risk, A number of studies have looked at how NSCLC patients' clinical responses are related. patients and the ratio neutrophil to lymphocyte (NLR)[11].

CXCL14 chemokine is essential for the tumor cell MHC-I expression upregulation, in the fact that although CXCL14 is quite similar to CXCL1 and CXCL8, it is not as frequent as the other CXC chemokines and does not interact with the receptor that they share, CXCR2. Due to the incomplete characterization of its native receptor, CXCL14 chemokine is considered an orphan chemokine[12]. It has been reported that chemokine ligand 14 CXCL14 chemokine is linked to various types of cancer cell migration and invasion. Nevertheless, how CXCL14 works and what receptor it binds to in the spread of lung cancer has been the subject of a limited number of studies[13].

Hyperlipidemia was shown to elevate cancer risk, with cancer cells often accumulating significant cholesterol through increased biosynthesis or enhanced absorption, thereby promoting rapid tumorigenesis. Numerous malignant neoplasms exhibit variations in blood cholesterol levels, whether elevated or diminished[14].

The serum alanine aminotransferase to aspart aminotransferase (AST/ALT) ratio was generally reduced, although both were elevated in patients with chronic diseases. Incident cancer cases showed a higher baseline ratio[15].

2. MATERIALS AND METHODS:

2-1 The Patients groups and controls

This study received approval from a local medical ethics council, and prior to its commencement, all participants consented to the sharing of their personal information. The case-control research included 90 samples of lung cancer, which were collected from, Center of Karbala Health Al Hussain Oncology and Hospital of Imam Sadiq, Babylon Oncology Center (Babelon, Iraq).

The control group consisting of 90 individuals seemed to be in a good health. Participants were registered and given a file for recording their details, like names, weight, sex, height, age, and other relevant information, ensuring that their age and sex matched these of patient groups. Individuals with other chronic conditions, including diabetes, systemic immunological diseases, thyroid gland disorders and heart disease, were not included in the work.

2-2 Data Collecting

The period for sample collection spanned from February 2024 to September 2024, sanctioned by the ethical approvals from both the MOH under order 253/in 5/2/2024 and MOHSER 527/on 4/2/2024 in Iraq. Participants' blood was analyzed for various factors, including CXCL14 sourced from Melsin Company in China using ELISA, as well as the effects of neutrophils, lymphocytes, platelets, and the neutrophil-to-lymphocyte ratio (NLR). Additionally, assessments were made for hemoglobin, total cholesterol, and triglycerides using kits from Linear Company in Spain and France/BIOLABO, along with alkaline phosphatase (ALP) from France/Biolabo, aspartate aminotransferase (AST) alanine aminotransferase (ALT), from Cobas /Roche, and albumin via the method of BCG from Tunisia/Biomaghre.

2-3 Statistical analysis

To guarantee the accuracy of each data point, it was entered into a computer several times during an Excel verification process. Additionally, specific values were calculated using formulas. The variable was represented as "mean & (SD)" to facilitate comparisons between the small and non-small cell carcinoma groups, utilizing the t-test for this analysis. All statistical data for the variables were examined through IBM SPSS Statistic ver. 25, with significance determined at P leas than 05.

3. RESULTS

Generally, the total patients' number involved in the current work was 90, comprising 36 individuals with SCLC and 54 with NSCLC. Participants had an average age of 64.500 years, alongside 90 samples from healthy individuals. A significant difference was observed between the groups ($P < 0.05$). In comparisons, NSCLC stage four patients exhibited higher levels than those at stage three, as did SCLC stage four compared to stage three. When utilizing cxcl14 to assess SCLC stage four against NSCLC at the same stage, results indicated that SCLC stage four levels were greater than those of NSCLC. Similarly, when cxcl14 was used to compare stage three of both SCLC and NSCLC, SCLC stage three was found to be higher than NSCLC at that same stage.

The significant positive correlation observed in the lung cancer patient group between cxcl14 and various factors, including triglyceride (TG), total cholesterol, Alanine Transaminase (ALT), neutrophil to lymphocyte ratio (NLR), Alkaline Phosphatase (ALP), and Aspartate Transaminase (AST), was confirmed by the linear regression analysis. Conversely, a notable negative correlation was found between cxcl14 and high-density lipoprotein (HDL) and Hemoglobin levels (Hb) in relation to levels of serum of cxcl14 within the same patient group, as illustrated in table 3.

The biomarkers of chemokine CXCL14 demonstrated remarkable diagnostic accuracy in patients with small-cell carcinoma, with a cut-off value of 120.007 pg/mL predicting lung cancer small cell type, yielding a specificity of 0.704 and sensitivity of 0.944, resulting in an AUC of 0.846 (CI: 0.767-0.925; 95%, p = 0.000), as illustrated in Table 4 and Figure 2. In contrast, for non-small cell carcinoma patients, a cut-off value of 87.05450 pg/mL was found, which showed a sensitivity of 1.000 and a specificity of 0.710, with an AUC of 0.832 (95% CI: 0.750-0.914; p = 0.000), as presented in Table 4 and Figure 3.

Table 1 The comparison of parameters for groups of Patients and controls

Parameter		Groups of Patients **Mean ± SD**			p-value
		healthy group (3)	**Non-small cell ca (2)**	**Small cell ca. (1)**	
Male/Female **female %** **male%**		**68/22** **24.5** **75.5**	**40 /14** **26.0** **74.0**	**24/12** **33.4** **66.6**	
Age (years)		**60.177 ± 5.762**	**62.652 ± 7.211**	**64.111 ± 7.640**	**A 2.011** **B 0.486**
Hb (g/dL)		**13.958±2.93**	**11.723±2.705**	**11.201±1.660**	**A 2.51E-07** **B 2.63E-08**
WBC	**NEUT. 10^3/µl**	**2.664±1.282**	**6.935±3.241**	**10.084±5.235**	**A 1.64E-05** **B 0.003**
	Total 10^3/µl	**6.310±1.569**	**7.509±3.418**	**7.845±2.848**	**A 0.069** **B 0.060**
	N/L	**3.615±1.577**	**3.630±1.126**	**4.125 ±5.91**	**A 1.9E-06** **B 0.007**
	LYM. 10^3/µl	**2.205±0.812**	**1.974±4.288**	**2.527±0.984**	**A 0.352** **B 0.515**
PLT 10^3/µl		**217.620±52.54**	**291.020 ±93.33**	**299.200±75.01**	**A 0.000** **B 0.000**
T C(mmol/l)		**.4990 ± 0.861**	**4.070 ± 0.803**	**5.333 ± 0.802**	**A 0.002** **B 0.000**
TG (mmol/l)		**1.382±0.861**	**1.931 ± 0.469**	**2.464 ± 0.264**	**A0.000** **B0.005**
L D L. C(mmol/l)		**2.950±0.603**	**2.868± 0.585**	**3.702± 0.581**	**A 0.002** **B 0.000**
		.0610±0.320	**0.346 ± 0.291**	**0.480 ± 0.288**	**A 0.003**

H D L. C(mmol/l)				B 0.005
V L D L. C(mmol/l)	0.692± 0.141	0.878± 0.203	1.121± 0.160	A0.000 B0.004
AST (IU/L)	18.110±6.222	31.250± 8.235	49.500±15.351	A 4.07E-06 B 0.001
ALT(IU/L)	12.000±4.280	22.750±3.828	32.500 ±4.412	A0.000 B0.007
ALP(IU/L)	88.422±22.83	224.259±64.692	255.888±47.379	A4.54E-12 B 1.41E-11
AST/ALT	1.592±0.651	1.790±1.067	2.424±2.232	A 0.137 B 0.387
CXCL14	50.301±2.890	130.386± 10.939	133.371± 11.583	A 7.02E-17 B 1.56E-25

Data reported as Means±SD: standard deviation, Hb: hemoglobin, WBC: Wight blood cells, NEUT: neutrophils, LYM: lymphocytes, PLT: Platelets, N/L: neutrophils/ Lymphocytes, AST:aspartate aminotransferase, ALT: alanine aminotransferase, ALP: alkaline phosphatase, B=p-value (non -small cell ca.+healt), A= p-value (small cell ca. +healthy)

Table 2 Comparison of parameters (CXCL14) of the Non-Small ca. and small cell ca. (stages 4 and 3) with control

Parameter	Non-small cell ca.		The small cell ca		p-value
	Stage4	Stage3	Stage4	Stage3	
Total number	26	28	14	22	
Age (years)	62.251±8.881	62.932±9.920	66.421± 6.500	62.188± 5.980	E- 0. 188 F - 0. 857 G- 0. 251 H - 0. 810
Hb g/dL	11.675±2.122	11.753±1.762	11.144±1.812	11.663±1.075	E- 0. 511 F – 0. 919 G – 0. 572 H – 0. 873
NEUT. 10ˆ3/µl	8.658±1.320	5.505±1.016	15.328±4.521	6.727±1.902	E - 0. 001

WBC						**F - 1. 13E-06** **G - 0. 007** **H - 0. 071**
	Total 10^3/µl	7.560 **±3.624**	**8.106±3.087**	**8.957±1.993**	**6.827±3.033**	**E - 0. 091** **F - 0. 731** **G - 0. 324** **H - 0. 303**
	N/L	**4.191±0.776**	**3.181±1.181**	**4.966±1.458**	**3.593±1.607**	**E - 0. 082** **F - 0. 063** **G - 0. 229** **H - 0. 648**
	LYM. 10^3/µl	**2.141±0.5583**	**1.846±0.415**	**3.114±0.393**	**1.736±0.700**	**E - 6. 88E-05** **F - 0. 143** **G - 0. 000** **H- 0. 64809**
PLT 10^3/µl 100-450		**273.416±0.588**	**306.666±74.385**	**322.000±88.821**	**285.727±82.896**	**E - 0. 402** **F - 0. 409** **G - 0. 326** **H - 0. 482**
TC(mmol/l)		**4.125±0.744**	**3.980± 1.039**	**6.242±**0.977	**4.918± 0.770**	**E -0. 112** **F - 0. 583** **G - 1. 53E-09** **H- 0.**

					010
TG (mmol/l)	**2.150±0.485**	**1.746± 0.515**	**2.812±0.369**	**2.245± 0.297**	**E- 0. 021** **F - 0. 142** **G- 1. 21E-05** **H - 0. 004**
LD L. C(mmol/l)	**2.899±0.521**	**2.781± 0.727**	**4.970 ±0.684**	**3.422±0.539**	**E - 0. 114** **F - 0. 583** **G - 1. 53E-09** **H -0. 010**
H D L. C(mmol/l)	**0.297±0.268**	**0.370±0.3911**	**0.580±0.276**	**0.423±0.300**	**E - 0. 710** **F- 0. 557** **G - 0. 001** **H - 0. 55**
VLDL.C(mmol/l)	**0.950 ±0.220**	**0.813± 0.234**	**1.282±0.167**	**1.847±0.135**	**E - 0 . 024** **F - 0. 597** **G - 1. 21E-05** **H- 0. 004**
AST (IU/L)	**42.166±10.336**	**22.338±6.987**	**58.285±11.554**	**43.626±8.666**	**E - 0. 091** **F - 0. 002** **G - 0. 020** **H - 0. 015**
ALT(IU/L)	**29.416±9.210**	**15.600±5.785**	**32.142±6.221**	**32.818±9.624**	**E - 0. 951**

					F - 0. 049 G - 0. 803 H - 0. 020
ALP (IU/L)	**230.083±90.150**	**219.600±36.529**	**275.857±50.926**	**243.181±42.466**	**E - 0. 184** **F- 0. 710** **G - 0. 175** **H - 0. 153S**
AST/ALT	**2.085±1.513**	**1.555±0.425**	**3.642±3.199**	**1.649±0.795**	**E - 0.153** **F - 0. 261** **G - 0. 268** **H - 0. 725**
CXCL14	**141.702±3.295**	**121.333±3.983**	**144.862±5.457**	**126.058±7.172**	**E -1. 31E-05** **F -1. 08E-13** **G - 0. 198** **H - 0. 171**

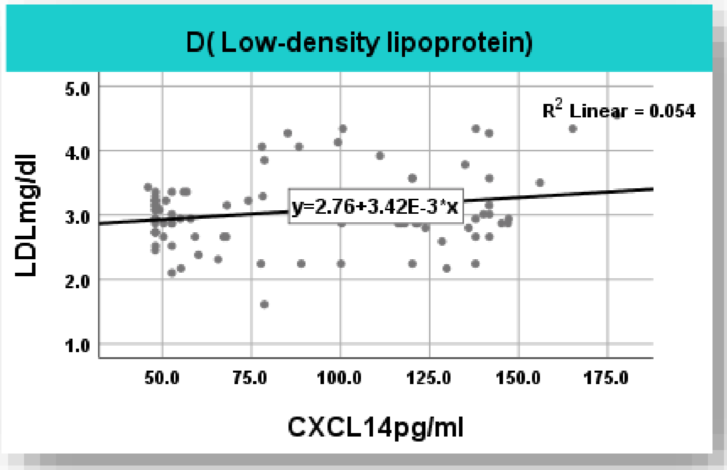
Data reported as Mean ±SD: standard deviation LYM: lymphocyte, WBC: Wight blood cells, Hb: hemoglobin, N/L: neutrophils/ Lymphocytes, NEUT: neutrophils, ALT: alanine aminotransferase, PLT: Platelets, ALP: alkaline phosphatase AST:aspartate aminotransferase, F=p.value of non-small cell ca. (stage 4+stage 3 E= p.value of small cell ca. (stage 4+stage 3), H= p.value (stage3 of non-small and small cell ca.

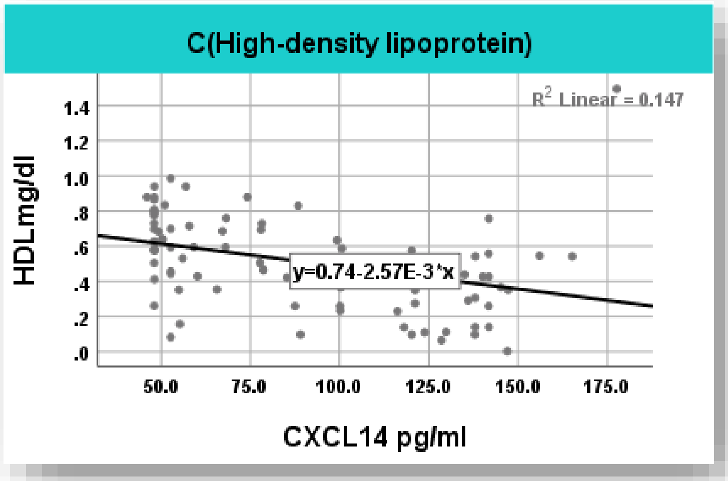
G= p.value (stage 4 of non-small and small cell ca.)

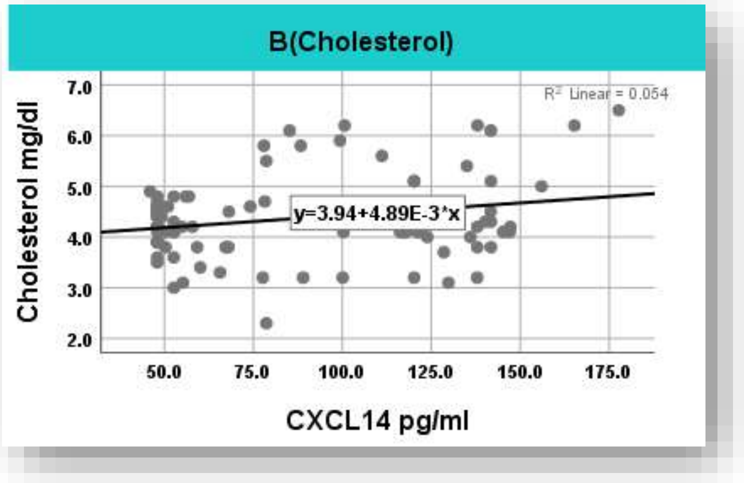
Table 3 The Correlation between the Studied Parameters Infected of Lung cancer and CXCL14

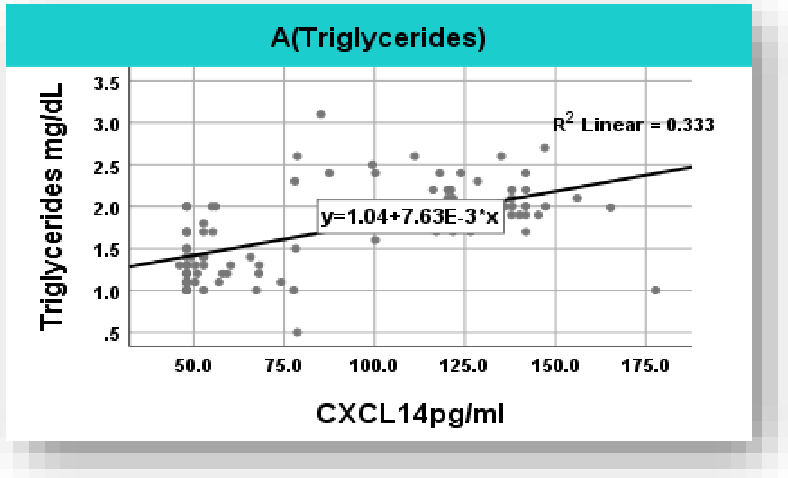
Parameter	p.value	r
Age (years)	**.**0141	**0.451**
LDL-Ch (mg/dL)	0.027	0.233^{**}
BMI kg/m^2	0.517	**0.491**
HDL-C (mg/dL)	0.000	-0.383^{**}
TC (mg/dL)	0.027	0.233^{**}
VLDL-C (mg/dL)	0.000	0.613^{**}

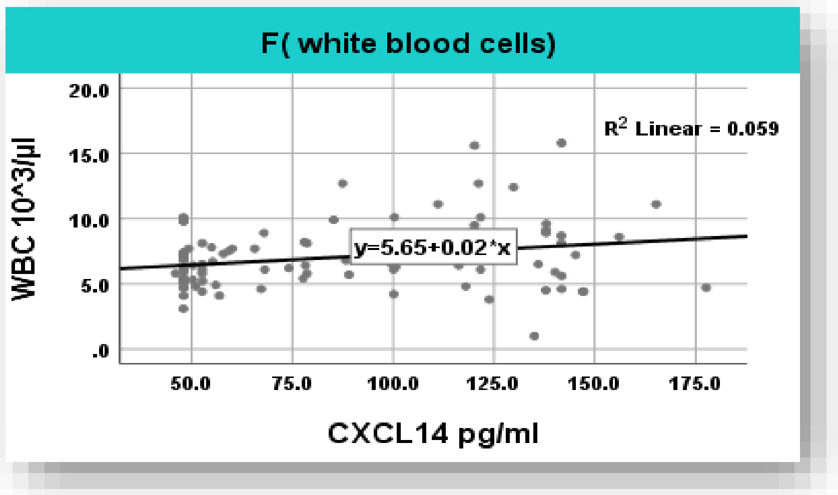
TG (mg/dL)	0.000	.0577**
Lymph. 10^3/µl	0.735	0.036
Ratio of N/L	0.000	0.701**
Total WBC 10^3/µl	0.021	.0243**
Neutro. 10^3/µl	0.000	0.620**
PLT 10^3g/L	0.000	0.603**
Hb g/dL	0.000	-0.530**
AST IU/L	0.000	0.546**
ALT IU/L	0.000	.0443**
ALP u/l	0.000	0.777**
AST/ALT	0.148	0.154

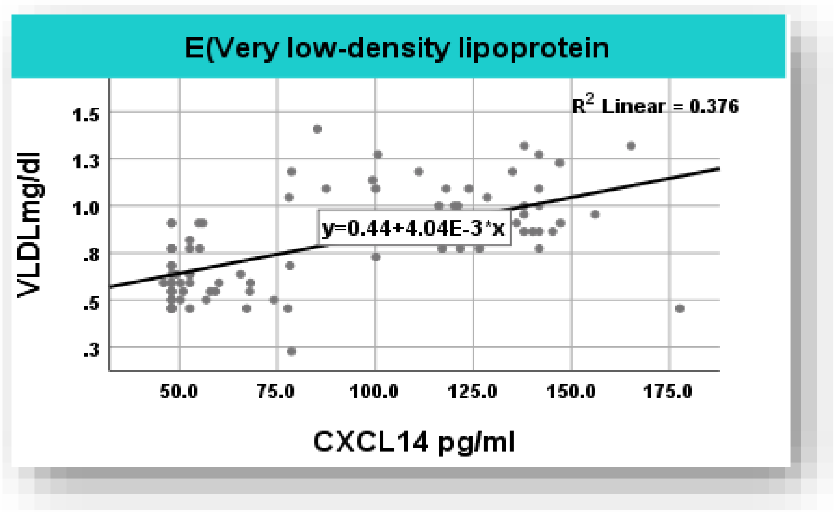


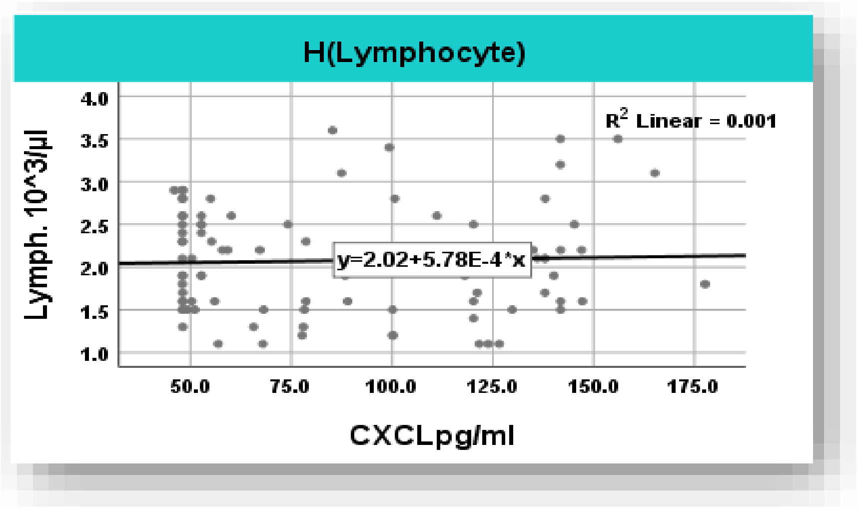


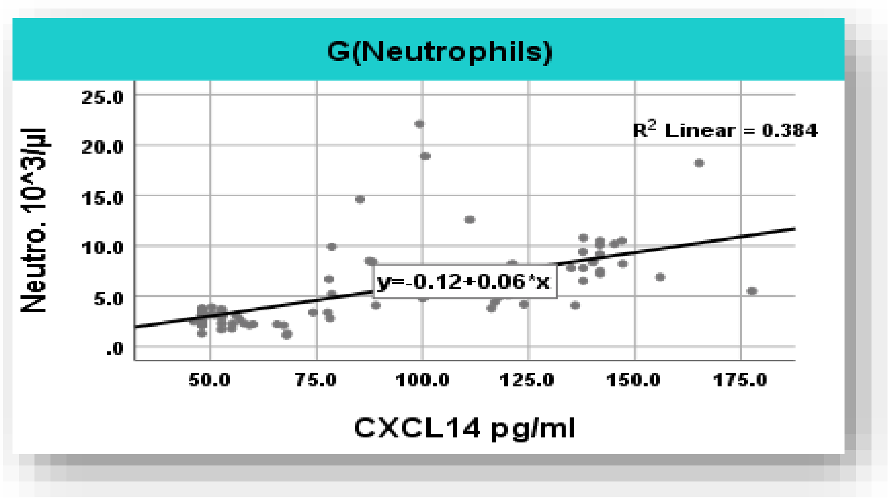

B(Cholesterol)
R² Linear = 0.054
y=3.94+4.89E-3*x
Cholesterol mg/dl
7.0
6.0
5.0
4.0
3.0
2.0
50.0
75.0
100.0
125.0
150.0
175.0
CXCL14 pg/ml

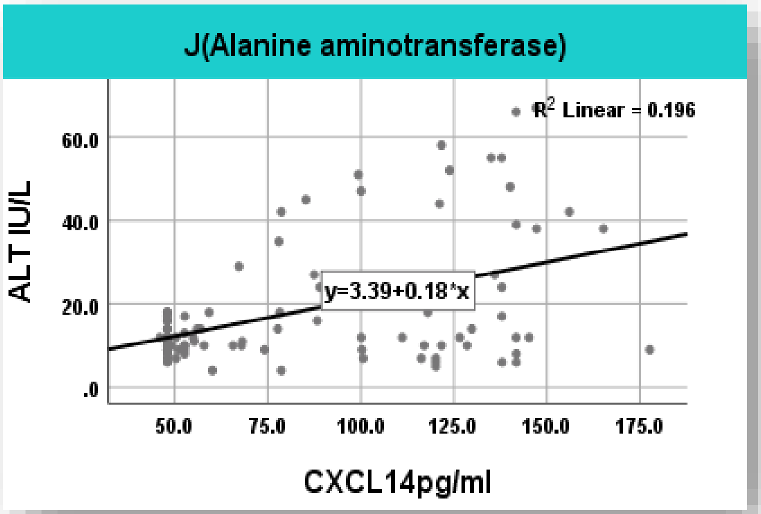

A(Triglycerides)
R² Linear = 0.333
y=1.04+7.63E-3*x
Triglycerides mg/dL
3.5
3.0
2.5
2.0
1.5
1.0
.5
50.0
75.0
100.0
125.0
150.0
175.0
CXCL14pg/ml

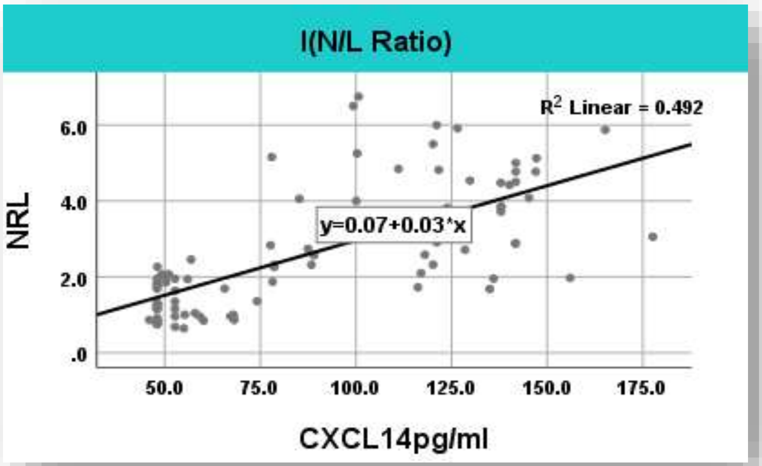

F(white blood cells)
R² Linear = 0.059
y=5.65+0.02*x
WBC 10^3/µl
20.0
15.0
10.0
5.0
.0
50.0
75.0
100.0
125.0
150.0
175.0
CXCL14 pg/ml

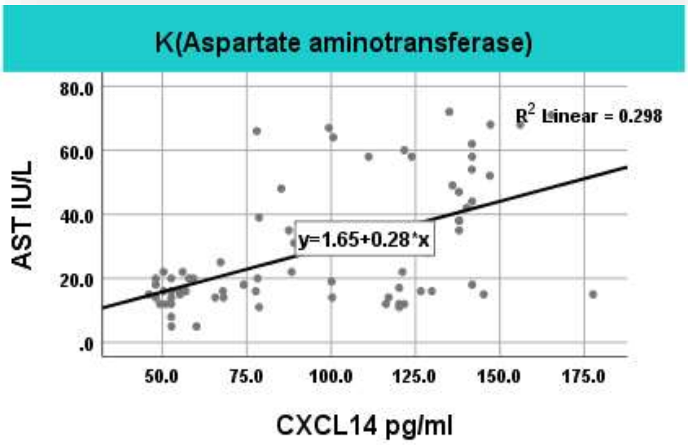

E(Very low-density lipoprotein
R^2 Linear = 0.376
y=0.44+4.04E-3*x
VLDLmg/dl
1.5
1.3
1.0
.8
.5
.3
50.0
75.0
100.0
125.0
150.0
175.0
CXCL14 pg/ml


H(Lymphocyte)
R^2 Linear = 0.001
y=2.02+5.78E-4*x
Lymph. 10^3/µl
4.0
3.5
3.0
2.5
2.0
1.5
1.0
50.0
75.0
100.0
125.0
150.0
175.0
CXCLpg/ml


G(Neutrophils)
R^2 Linear = 0.384
y=-0.12+0.06*x
Neutro. 10^3/µl
25.0
20.0
15.0
10.0
5.0
.0
50.0
75.0
100.0
125.0
150.0
175.0
CXCL14 pg/ml


J(Alanine aminotransferase)
R^2 Linear = 0.196
y=3.39+0.18*x
ALT IU/L
60.0
40.0
20.0
.0
50.0
75.0
100.0
125.0
150.0
175.0
CXCL14pg/ml


I(N/L Ratio)
R^2 Linear = 0.492
y=0.07+0.03*x
NRL
6.0
4.0
2.0
.0
50.0
75.0
100.0
125.0
150.0
175.0
CXCL14pg/ml


K(Aspartate aminotransferase)
R^2 Linear = 0.298
y=1.65+0.28*x
AST IU/L
80.0
60.0
40.0
20.0
.0
50.0
75.0
100.0
125.0
150.0
175.0
CXCL14 pg/ml

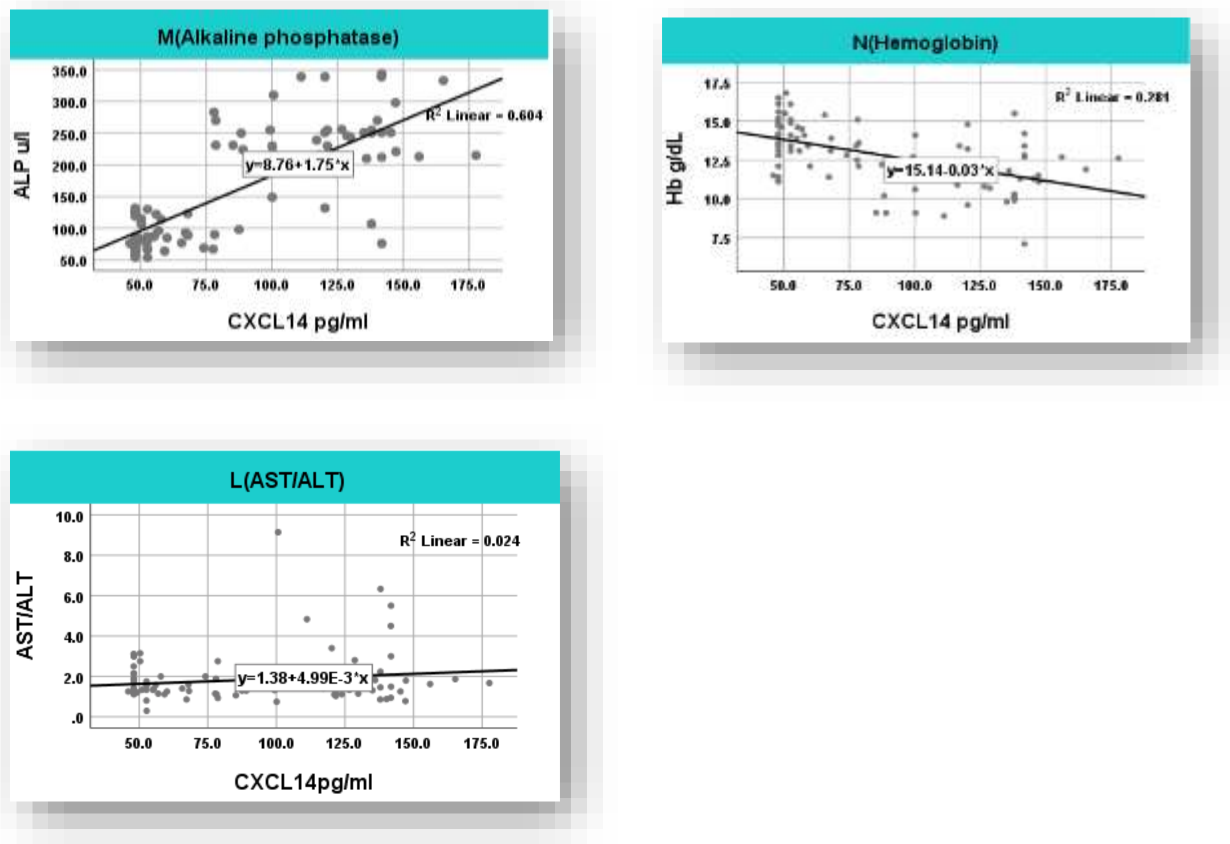


Figure (1) The analysis of linear regression among level of serum of studied CXCL14 with other parameters where (A: TG, C: TC, B: HDL, E: VLDL, D: LDL, F: WBC, H: Lymph., G: Neut., J: ALT, I: NRL, K: AST, M: ALP, L: AST/ALT, N: Hb.

Table (4) ROC-Area under Curve Analysis of the Measured Biomarkers in Small Cell Carcinoma Patients

Variable	Specficity %	Cut-off concentration	Senstivity %	95% CI of AUC	AUC	p-value
CXCL14 pg/ml in non-small cell ca	**0.710**	87.05450	**1.000**	**0.750**-0.914	**0.832**	0.000
CXCL14 pg/ml in small cell ca.	0.704	120.007	0.944	**0.767**-0.925	**0.846**	0.000

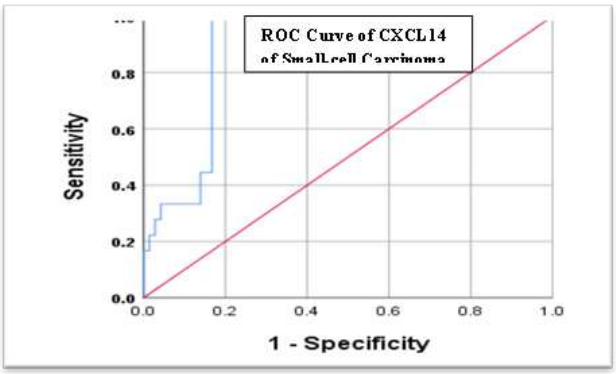


Figure 2 The ROC Curve of CXCL 14 showing Recognition of Small-cell Carcinoma Patients Group.

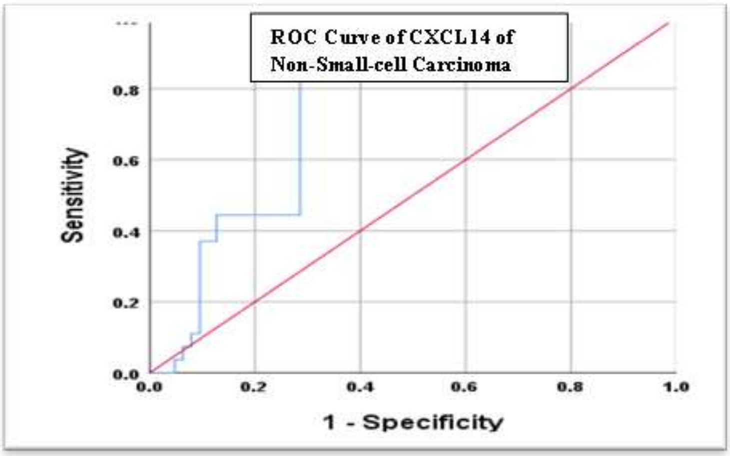


Figure 3 The ROC Curve of CXCL 14 showing Recognition of Non-Small-cell Carcinoma Patients Group

4. DISCUSSION

CXCL14 is expressed in multiple organs, indicating its role in maintaining systemic homeostasis. This chemokine is highly present along the intestinal lining and exhibits significant gene silencing in clinical samples of colon cancer. Such silencing suggests a potential link between CXCL14 suppression and the ability of cancer cells to evade immune responses[16]**.**

Marked disparities in a regulation of (CXCL-14) expression were seen in human colorectal carcinoma neoplasms and murine colon cancer models. Clinical tumor tissues frequently exhibit silencing of CXCL14, but new tumors in mice demonstrate upregulation of the gene[17]. A clinical tumor sampls we examined are the product of clonal differentiation, extensive mutations, and prolonged in vivo selection. Human tumor tissue frequently grows over several years or even decades before detection[18]**.** Conversely, mouse tumor samples are primary tumors that evolve over months, allowing less opportunity for mutation and selection. Consequently, the stages of malignancy vary between mice and humans. Secondly, it is crucial to acknowledge that the expression of CXCL14 diminishes as cancer cells increase in malignancy. Nonetheless, CXCL14 expression is elevated in specific cancers[19].

Some studies in lung cancer patients have observed elevated levels of CXCL14, CXCL13, and CCL20 and compared them with controls to identify inflammatory factors. Therefore, CXCL14 was initially proposed as a potential diagnostic marker for lung cancer[20]

Hyperlipidemia was demonstrated to elevate a risk of cancer. Cancer cells typically amass substantial quantities of cholesterol by upregulating cholesterol production or augmenting cholesterol absorption, resulting in accelerated cancer progression. Variations in blood cholesterol levels (either declines or elevations) are significant occurrences in numerous cancers[21]. Research indicates that the cholesterol levels in tissue cells associated with breast, ovarian, and kidney cancers are elevated. The overproduction of LDLR is a critical mechanism enabling cancer cells for obtaining more necessary fatty acids via LDLR endocytosis. Research indicates that in the majority of malignancies, the overexpression of LDLR facilitates the accelerated uptake of LDL. In normal human prostate cells, LDLR expression is modulated by feedback regulation of LDL-C levels, whereas this regulatory feedback is typically lacking in prostate cancer cells[22;23]**.**

The growth of breast cancer is positively correlated with low-density lipoprotein cholesterol (LDL-C), which is a kind of unhealthy cholesterol. Based on the findings of a prospective research conducted in Portugal, it was shown that breast cancer patients who had higher levels of LDL-C at the time of diagnosis had tumors that were bigger, more differentiated, and developed more quickly. LDL-C levels in the plasma were shown to have a positive correlation with tumor volume[24].

Our purpose was to study the link between distinct lipid profiles and various cancer locations. We noted a propensity for an inverse correlation between HDL levels and cancers of the digestive organs, breast, skin, urinary tract, and lymphoid and hematopoietic tissues; however, the relatively small sample sizes precluded the determination of significant associations in site-specific cancer analyses. Furthermore, we noted a trend indicating a favorable correlation between total cholesterol and cancers of the respiratory organs and urinary system.[25]**.** In the Atherosclerosis Risk in Communities (ARIC) study cohort, we found that low levels of HDL-cholesterol correlated with an increased incidence of lung cancer among former smokers and in the whole population. Certain investigations identified a slight inverse correlation between HDL-cholesterol levels and the incidence of lung cancer[26]

This study revealed a notable positive correlation between cholesterol levels and lung cancer patients, with the exception of HDL cholesterol, which showed a negative association. Additionally, cholesterol levels varied with the type and stage of lung cancer, being elevated in patients with small-cell lung cancer compared to those with non-small-cell lung cancer.

Many recent studies have demonstrated a correlation between mortality and the “AST/ALT” ratio. Furthermore, an elevated “AST/ALT” ratio was an independent one-year predictor of polymyositis/dermatomyositis-associated interstitial lung disease[27]**.** Likewise, a higher “AST to ALT” ratio has been associated with mortality from all causes, especially cardiovascular disease. Studies related to cancer survival have shown that an elevated “AST/ALT” ratio is associated with a poor prognosis in renal cell carcinoma, head and neck cancer, oral cavity and oropharyngeal cancer, and other types of cancer[28]**.**

Understanding the mechanisms underlying its development and progression is essential, as lung cancer remains the most common malignancy and the leading cause of cancer-related deaths worldwide. Studies suggest that inflammation plays a significant role in the occurrence of various cancers. Neutrophils are not only key players in the inflammatory response but also integral components of the tumor microenvironment. Tumor-associated neutrophils (TANs) infiltrate tumors and actively contribute to their growth and progression. Moreover, they impact the therapeutic response and prognosis of lung cancer by modulating the immune microenvironment[30].

5. CONCLUSION

This study examines the relationship between chemokine CXCL14 and lung cancer among patients with “small and non-small cell carcinoma” as well as healthy individuals. An increase in chemokine CXCL14 was observed in patients with stage four “non-small cell carcinoma” and stage four small cell carcinoma. Additionally, it was noted that small-cell carcinoma at stage 3 exhibited higher levels than non-small cell carcinoma. This research elucidates how CXCL14 facilitates the metastasis of lung cancer, potentially linking to signaling pathways that lead to cellular migration. Furthermore, serum levels of chemokine CXCL14 may serve as promising early diagnostic performance indicators for lung cancer, meriting further investigation.

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