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Evaluation the impact of IL-17 level in pulmonary carcinoma patients

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***Abstract*---**The cancer burden continues to grow globally, exerting tremendous physical, emotional and financial strain on individuals, families, communities and health systems, immune dysfunction is an important cause of tumor development. A case -control study aimed to assess the role of IL-17 serum level in pathophysiology of lung cancer patients.150 patients attending to Middle Euphrates Cancer Center in AL-Najaf province from September till December 2021 that included 6(4%) small cell carcinoma patients and 144 (94 %) non small carcinoma patients from which squamous cell carcinoma patients represent 72(48%), Adenocarcenoma 48(16 %) and large –cell lung carcinoma 24(16%). as well as 30 apparently healthy subjects as control group . Two ml of vien blood were collected from all subjects put in gel tube to separate serum that used to estimate the IL-17 level by ELISA. The results showed a significant increase ($P<0.05$) in serum concentration of IL-17 in lung cancer patients compare to healthy subjects. According to stage of lung cancer the concentration of IL-17 increased with severity of disease and this considar as biomarker for prograssve of state. The current study concluded that the disease affects the body's immune response represented by increased the level IL-17 and correlated with severty of disease.

***Keywords*---**IL-17, lung, cancer, grade, stage.

Introduction

Pulmonary carcinoma is a malignant lung tumor described by the abnormal proliferation of cells that occurs in lungs, its leading cause of cancer morbidity and mortality in men, whereas, in women ranks third for incidence, after breast and colorectal cancer, and second for mortality, after breast cancer (Sung *et al.*,

2021). In 2020, an estimated 2.2 million new cancer cases and 1.8 million deaths, lung cancer is the second most commonly diagnosed cancer and the leading cause of cancer death, representing approximately one in 10 (11.4%) cancers diagnosed and one in 5 (18.0%) deaths. In Iraq, the incidence for 2020 amounted to about 2548 (7.5) and mortality to about 2326 (11.8) (IARC, 2020). A major classes of lung cancer are : small cell lung carcinoma (SCLC) and non-small cell lung carcinoma (NSCLC) , non-small cell carcinoma has three main categories, squamous cell carcinoma, adenocarcinoma and large cell carcinoma (Nicholson *et al.*, 2021). Immune dysfunction is an important cause of tumor development.Th17 lymphocytes are a subpopulation of helper CD4+ T cells that secrete cytokines such as interleukin IL-17A, IL-22, IL-6 and IL-1 that mediate harmful effects in the lung cancer with enhancing immune-mediated inflammatory responses. IL-17 are highly expressed in patients with NSCLC that promote microvasculogenesis in the tumor microenvironment and induce tumor cell growth and metastasis.(Chen *et al.,* 2020) . Proinflammatory cytokine IL-17 directly or indirectly promotes tumor angiogenesis and cell proliferation and that it inhibits apoptosis via the activation of inflammatory signaling pathways; IL-17 therefore contributes to the progression of lung cancer.

Methods

A Case - control hospital based study was adopted, during the period January-June2021 . 150 patients attending Middle Euphrates Cancer Center in AL-Najaf province from September till December 2021 that included 6(4%) small cell carcinoma patients and 144 (94 %) non small carcinoma patients from which squamous cell carcinoma patients represent 72(48%) , Adenocarcenoma 48(16 %) and large –cell lung carcinoma 24(16%). as well as 30 apparently healthy subjects as control group . 2 ml of Blood were collected from all subjects put in gel tube to separate serum and kept at -20 ◦ C used to evaluated IL-17 by ELISA system (Elabscience \ USA).

Inclusion and Exclusion Criteria

Patients suffering from lung cancer were included while patients with chronic disease , other type of cancer , pneumonia , RTI were excluded

Ethical considerations

The study concept was accepted by Institutional Ethics Committee for Human Studies from AL-Sadar Hospital and the College of Science at Kufa University. In addition, all of the subjects provided written informed consent prior to participating in the research.

Statistical analysis

The one-way ANOVA Scheffe's method was employed represented as mean ±standard deviation (S.df) . A $p < 0.05$ was considered statistically significant to compare between patients and healthy.

Result and Discussion

Demographic characteristics for 150 patients

Attending to Middle Euphrates Cancer Center in AL-Najaf province by patients-control study revealed that male were 96(64)% and female were 54(36)% and the statically analysis revealed a significant difference between male and female, as shown in Table 1.

Table 1: Distribution of patients according to sex, age and type of lung cancer

Variable	Group	N	%	Healthy group	%
Sex	Male	96	64	18	60
	Female	54	36	12	40
Age (years)	< 40			5	16.6
	40 - 50	24	16	3	10
	51 - 60	42	28	7	23.3
	61 - 70	48	32	9	30
	71 - 80	30	20	4	13.4
	81 - 90	8	4	2	6.7
Pathological Type	Squamous Cell Carcinoma	72	48		
	Adenocarcinoma	48	32		
	Large-cell Lung Carcinoma	24	16		
	Small Cell Carcinoma	6	4		

In local study, (Abdul-Zahra and Taiban, 2021)founded that the percent of males 67% were more than females 33% in Al-Najaf province. Also, another study also indicated that male were outnumber 70% than female and the age between 60-69 were high frequency 37.7% followed by 27.7% for patients with age between 50-59 also, observed that 63.3% of patients (Albadri *et al.*, 2019).

Increase risk of lung cancer in smoking persons more than non-smokers, and in male more than females and in the age groups (50 years and above). This may be due to higher percentage of smoking in males, passive smoking , type of occupational exposure and other risk factors are more in the males than in the females(Jasim & Bahir, 2020). The lack of any appreciable sex difference in the rats of lung cancer is surprising given men' s greater cumulative exposure to smoking, in most populations, compared with women. In addition, men have a greater exposure to other risk factors for lung cancer including occupational carcinogens. Men also smoke more cigars and pipes,3 take longer puffs of longer duration and leave shorter butts compared with women(Keeffe *et al.*, 2018).

Older age is associated with cancer development due to biologic factors that include DNA damage over time and shortening telomeres. Accordingly, the median age of lung cancer diagnosis is 70 years for both men and women. Approximately 53% of cases occur in individuals 55 to 74 years old and 37% occur over 75 years

old. The highest incidence of lung cancer in men is 585.9 per 100,000 in 85–89 years old, while the highest incidence in women is 365.8 per 100,000 in 75–79 years old. Lung cancer is the leading cause of death by any means in men over 40 years and in women over 59 years of age(Thandra *et al.*, 2018). In other hand the result appear that NSCLC more than SCLC this agree with (Scagliotti et al., 2022) observed that non-small cell lung cancer (NSCLC) accounts for ~ 85% of all lung cancers and has multiple histological subtypes including adenocarcinoma and central squamous cell carcinoma. Also , (Fuentes et al., 2021) confirmed that small cell carcinoma accounts for about 20% of cases while non-small cell carcinoma comprises 80% of lung malignancy. Also (Schabath & Cote, 2019) they found NSCLC represents more than 80 - 85% of lung cancers of lung cancers of which approximately 40% are adenocarcinoma, 25% to 30% are squamous cell carcinoma, and 10% to 15% are large cell carcinomas. (Lukeman, 2015) confirmed that the two main types of lung cancer are treated completely differently about 80% to 85% of lung cancers are NSCLC. The main subtypes of NSCLC are adenocarcinoma, squamous cell carcinoma, and large cell carcinoma and about 10% to 15% of all lung cancers are SCLC and it is sometimes called oat cell cancer.

Distribution the Patients According to Stages of lung cancer

The study revealed that patients divided according to stages to Stage I-II were 50(33%) , 42 (28%) Stage III and 58 (39 %) Stage IV. (Figure 1).

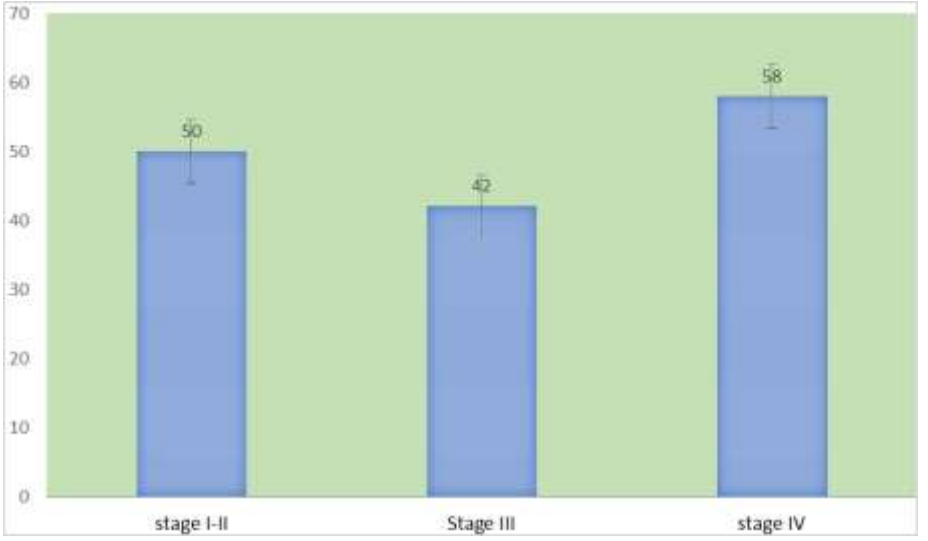

Figure 1: Classification of lung cancer patients according to stage

(Oser *et al.,* 2015) They found that more patients with stage IV than patients with stage III and stage I,II of lung cancer. (Status & Developments, 2013) confired that approximately 70% of patients present with advanced stage NSCLC. (Reck *et al.*, 2013) found that more than half of the NSCLC cases were already at Stage IV disease (Stage IV-58.2%). Only 7.5% of cases were diagnosed in Stage I and 4.8% in Stage II while for small cell carcinoma cases, 58% were at the extensive stage at time of diagnosis.

Evaluation concentration of IL-17 according to stage of diseaes

The results revealed that serum level of IL-17 was increased in Stage III and stage IV (132.61 ± 40.58 , 168.93 ± 23.75) pg/ml higher than stage I -II (103.48 ± 29.82) pg/ml as show in figure 2.

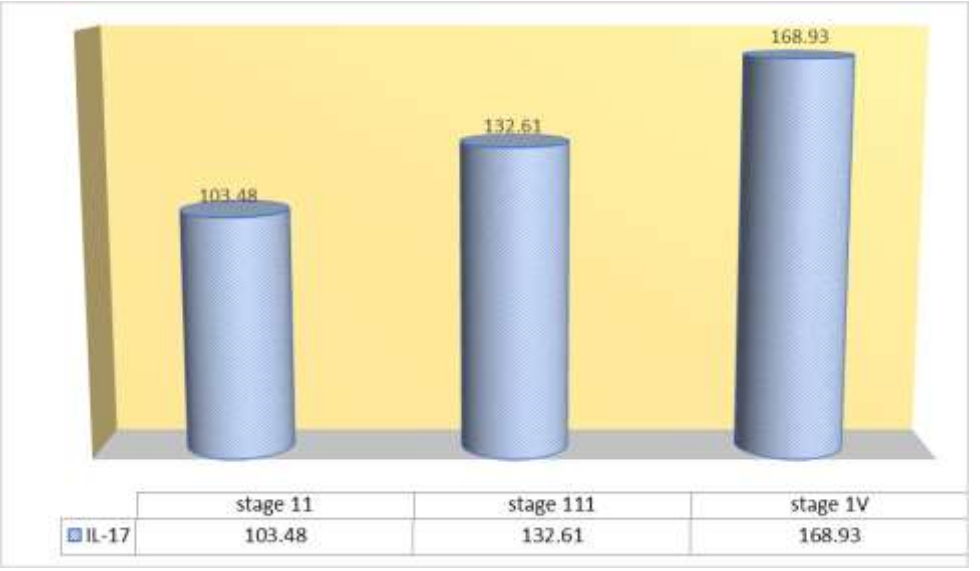

Figure 2: IL-17 level according stage in lung cancer patients

Zhang *et al.*, (2012) observed that IL-17 was correlated with tumor progression and posativly associated with TNM staging of NSCLC patients. (Zeng *et al.*, 2015) showed that high IL-17 expression was significantly correlated with an advanced stage of NSCLC (III/IV) . In same line (Chen *et al.,* 2020) suggested that IL-17 serum level was higher in patients with stage III and IV cancers which recorded mean value (9.6 , 14.49 pg/ml) than stage 11 with mean (5.6 pg/ml). IL-17 were higher in patients with squamous cell carcinoma than in patients with adenocarcinoma.

Evaluation IL-17 levels in patients and healthy controls:

The result suggested that the serum level of IL-17 in lung cancer patients (136.50 ± 32.97) pg/ml was significantly higher than healthy controls (18.84 ± 2.85) pg/ml as shown in Figure 3.

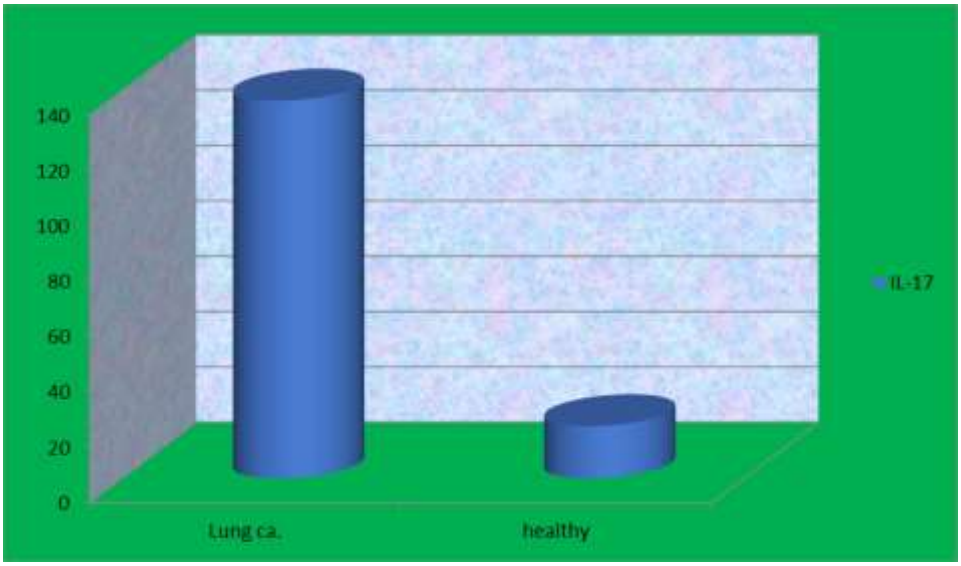

Figure 3: Serum level in lung cancer patients and healthy

Wu *et al.* (2016) demonstrated that IL-17 promotes the development of lung cancer and explain that IL-17 contributes to the metastasis and progression of lung cancer. (Cancer, 2013) founded an increased IL-17RA serum level in lung cancer patients and observed eleveated level in metastasis cases more than patients without metastasis. Also (Pan *et al.*, 2015) showed that IL-17 was significantly higher in tumour tissues than in adjacent tissues and distant normal lung tissue.

Estimation serum level of IL-17 according to type of lung cancer

This results clearly demonstrated that IL-17 was signifecantly increased in non-small cell lung carcinoma (180.36 ± 43.15) pg/ml then in small cell carcinoma (97.11 ± 20.45) pg/ml. According to type of non small cell carcinoma , the squamose cell carcimona recorded (196.67± 32.55) pg/ml, adenocarcinoma and large cell carcinoma recorded (134.73 ± 20.45 , 116 .33 ± 29.87) pg/ml respectively (Figure 4).

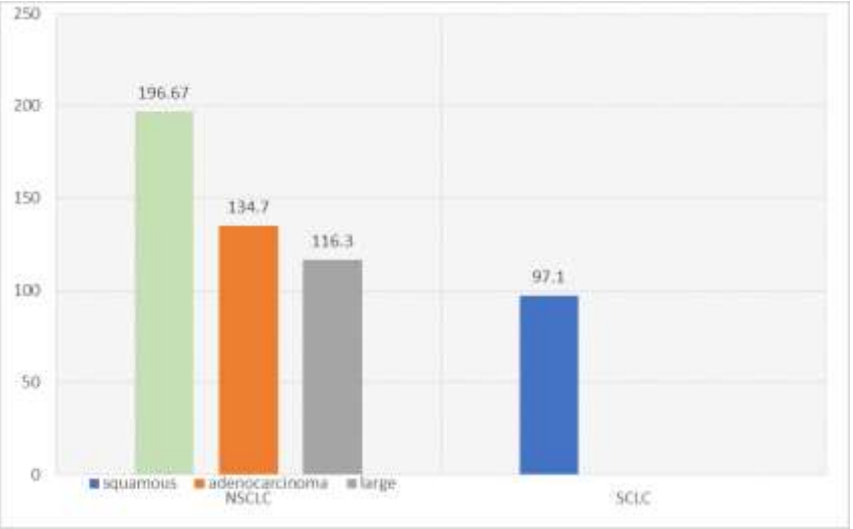

Figure 4: IL-17 serum level according to type of lung cancer

This results agree with study by(Chen *et al.*, 2020) found that IL-17 elevated in patients than in healthy (8.32 vs 5.36 pg/ml and demonstrated that IL-17 play an important role in the development of NSCLC in patients with higher elevation in squamous cell carcinoma patients than in those with adenocarcinoma. Joerger *et al.* (2016) confirmed that IL-17 concentration in the peripheral blood were significantly higher in the NSCLC group than in the control group and may act as markers for treatment of NSCLC. Also, (Song *et al.*, 2019) observed that IL-17 are highly expressed in patients with NSCLC. (Wei *et al.,* 2018) They note that IL-17 is significantly more expressed in patients with NSCLC than in patients with SCLC. Xu *et al.* (2014) observed high serum levels of IL-17 evidence indicated that these cytokines contributed to the growth and spread of lung cancer, increasing evidence has suggested that IL-17 expression was elevated in NSCLC and IL-17 can promote tumor progression via an increase in angiogenesis and prevent cancer cells from immune surveillance. Qian *et al.* (2015) shown that IL-17 is highly expressed in tumor tissues of non-smallcell lung cancer (NSCLC), with the levels of IL-17 expression positively correlating with the aggressiveness of the malignancy and demonstrated that IL-17 might play an oncogenic role by inhibiting tumor cell apoptosis, impairing antitumor responses, promoting tumor angiogenesis and promoting tumor metastasis and invasion (Suryasa et al., 2021).

Xu *et al.* (2014) confirmed that serum IL-17 level were significantly elevated in patients with NSCLC (21.34± 9.26 pg/ml) compared with control subjects (11.12±2.83 pg/ml) making them potential adjunctive tools for diagnosis of lung cancer (p50.01). Nicola *et al.* (2021) they demonstrated that IL-17 was significantly higher in patients with NSCLC than controls, and their levels significantly correlated with tumour size. Nicola *et al.* (2021) observed that increased serum IL-17 level in samples of patients with neoplastic disease with related to the spread of malignancies in lung cancer and concludedthat increased number of IL-17-producing cells in neoplastic tissue with asossiated to poor survival and increased lymphangiogenesis in non-small cell lung cancer (NSCLC).

Conclusions

The current study concluded that the disease affects the body's immune response represented by increased the level IL-17 and correlated with severty of disease.

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