

Estimation of the Leptin Hormone and Some Biochemical Variables in Patients with Lung Cancer in Kirkuk Province

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Abstract

This study aimed to estimate the level of leptin hormone and some biochemical variables in patients with lung cancer. Twenty five patients with lung cancer and 24 healthy control were enrolled in this study. The results showed a significant decrease in the level of leptin in patients with lung cancer compared to healthy control. In group of patients with lung cancer who had BMI (20 – 23 kg/m²), (24–26 kg/m²), (more than 30 kg/m²) the levels of leptin were (1.42 ± 0.54), (4.35 ± 2.19), (8.75 ± 1.2) ng/ml respectively, comparing with the healthy control (4.89 ± 1.29), (6.85 ± 1.49), (9.85 ± 2.62) ng/ml respectively. The results also showed that there was a significant increase in activity of ALT in patients group (30.8 ± 16.4) U/L compared to healthy control (22.8 ± 6.55), while there was no statistically significant differences in the activity of AST in patients group (25.4 ± 8.9) U/L compared to healthy control (27 ± 9.2). There were no statistically significant correlation between leptin level with ALT (r = -0.104) and AST (r = 0.092).

Keywords: Lung cancer, Leptin, Body mass index BMI.

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تقدير هرمون اللبتين وبعض المتغيرات الكيموحيوية في المرضى المصابين بسرطان الرئة في محافظة كركوك

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الملخص

هدفت هذه الدراسة إلى تقدير مستوى هرمون اللبتين وبعض المتغيرات الكيموحيوية في مرضى سرطان الرئة. شملت هذه الدراسة 25 مريضاً بسرطان الرئة و 24 شخصاً سليماً تم تسجيلهم كمجموعة سيطرة. أظهرت النتائج انخفاض في مستوى اللبتين في مرضى سرطان الرئة مقارنة مع مجموعة السيطرة. في مجاميع مرضى سرطان الرئة ذوي مؤشر كتلة جسم ($20 - 23 \text{ kg/m}^2$), ($24 - 26 \text{ kg/m}^2$), (more than 30 kg/m^2) كانت مستويات اللبتين ± 1.42 ng/ml 0.54 , (2.19 ± 4.35) , (1.2 ± 8.75) على التوالي، بالمقارنة مع مجموعة السيطرة التي كانت 4.89 ± 6.85 ng/ml 1.29 , (1.49 ± 9.85) , (2.62 ± 9.85) على التوالي. النتائج أيضاً أظهرت ارتفاعاً معنوياً في فعالية إنزيم ALT في مجموعة المرضى حيث كانت (16.4 ± 30.8) U/L بالمقارنة مع مجموعة السيطرة (6.55 ± 22.8) ، بينما لم يكن هناك فرق معنوي ذو دلالة احصائية في فعالية إنزيم AST في مجموعة المرضى التي كانت (8.9 ± 25.4) U/L مقارنة مع مجموعة السيطرة (9.2 ± 27) . لم تكن هناك علاقة ارتباط ذات دلالة احصائية معنوية لمستوى اللبتين مع إنزيم ALT $(r = -0.104)$ وكذلك مع إنزيم AST $(r = 0.092)$.

الكلمات الدالة: سرطان الرئة، هرمون اللبتين، مؤشر كتلة الجسم.

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1. Introduction:

Lung cancer is a cancer of the modern man and only few cases date before the 20th century. By the mid-twentieth century it had swept the world, due to increased worldwide tobacco consumption [1]. Lung cancer remains the leading cause of cancer mortality worldwide, and while mortality is gradually decreasing in high-income countries for most cancers, lung cancer mortality is not decreasing and is actually increasing in women [2]. Lung cancer is a malignant tumor in the tissue of human lungs [3], it is uncontrolled growth of altered cells which may begin in one or both lungs. Most often the cells that line the air passage are affected [4]. Lung carcinoma begins from the epithelial cells of the bronchi and develops into hyperplasia, metaplasia, dysplasia, carcinoma in situ and then to invasive cancer [5].

The relationship between obesity and certain types of cancers makes leptin a target for research in other types of cancer [6]. Leptin is a polypeptide hormone consisting of 167 amino acids with a molecular weight of 16 kDa [7], it is composed of four chains of helices- α and two short β -type bands [8] and it is characterized by an intramolecular disulphide bond responsible for the biological action of hormone [9]. The leptin hormone was detected in 1994 by Friedman, and the word leptin came from 'leptos', a Greek word meaning thin [10]. Leptin is produced primarily in white adipose tissue [11] and it is also synthesized by brown adipose tissue, ovaries, stomach, bone marrow, liver and skeletal muscle [12]. The function of leptin is to regulate the energy balance in the human body by monitoring energy expenditure and energy intake through its biological effect on the arcuate nucleus of the hypothalamus [13]. Leptin play a significant role in innate and acquired immunity and induces chemotaxis of neutrophil cell and enhance phagocytosis [14]. There is a hypothesis that dysfunction of leptin may increase the risk of cancer development [15].

The process of proliferation and spread of cancer cells are accompanied by changes in many of the biochemical variables which include proteins, hormones and enzymes [16], previous studies have shown a link between cancer and the aminotransferases, which are liver enzymes which include aspartate amino transferase AST and alanine amino transferase ALT [17]. The present study was designed to determine leptin levels in patients with lung cancer, as well as to determine the effect of lung cancer on the level of liver enzymes.

2. Subjects and Methods:

Twenty five patients with lung cancer were enrolled in this study, they were admitted to Kirkuk Oncology and Hematology Center between September 2016 and March 2017. The control group included 24 healthy people, they were between the ages of 32 to 64. The weight and height of the subjects studied were measured by an electronic balance for the purpose of obtaining body mass index (BMI) values. Body Mass Index (BMI), which is measured as $[(\text{weight in kilogram} / (\text{height in meter})^2)]$, and designate to be a simple measurement of population-level for obesity, and it is an indicator to classify obesity, overweight and underweight in adult people [18]. Blood samples 3 ml were collected from the patients and from the healthy control, the blood was placed in plain tubes and left to clot at room temperature for 10 minutes, and then centrifuged at 1056 xg for 10 minutes and then sera were dispensed into tubes and used for measuring of the study parameters. The levels of leptin were estimated using a human Leptin kit processed by Labor Diagnostika Nord-Germany, which was made using Enzyme-Linked ImmunoSorbent Assay (ELISA). AST, ALT enzymes activity were estimated according to the standard operating procedures of colorimetric method using kit supplied by (BIOLABO/France).

2.1 Statistical analysis :

statistical analysis was performed using SPSS-21 (statistical package for social sciences version 21), data were analyzed by using one-way ANOVA. Duncan test was used to assess significant difference among means. Correlations between parameters were performed using Pearson's correlation coefficient (r). The values are expressed as mean and standard deviation, a ($P \leq 0.05$) was considered statistically significant.

3. Results and discussion:

As shown in [Table 1](#), the patients and healthy control were divided into three groups depending on body mass index; ($20-23 \text{ kg/m}^2$), ($24-26 \text{ kg/m}^2$) and ($\text{more than } 30 \text{ kg/m}^2$). In this study, it was found that leptin level was low in patients group who had BMI ($20 - 23 \text{ kg/m}^2$), ($24-26 \text{ kg/m}^2$) compared to the healthy control, and the lowest level of leptin was found in the group of patients who had a low BMI ($20-23 \text{ kg/m}^2$), in this group it was found that leptin level for lung cancer patients was ($1.42 \pm 0.54 \text{ ng/ml}$) while its level in the healthy

group was $(4.89 \pm 1.29 \text{ ng/ml})$ as shown in Fig.1. A previous study has shown that leptin levels were significantly lower in patients with lung cancer than in healthy control [19].

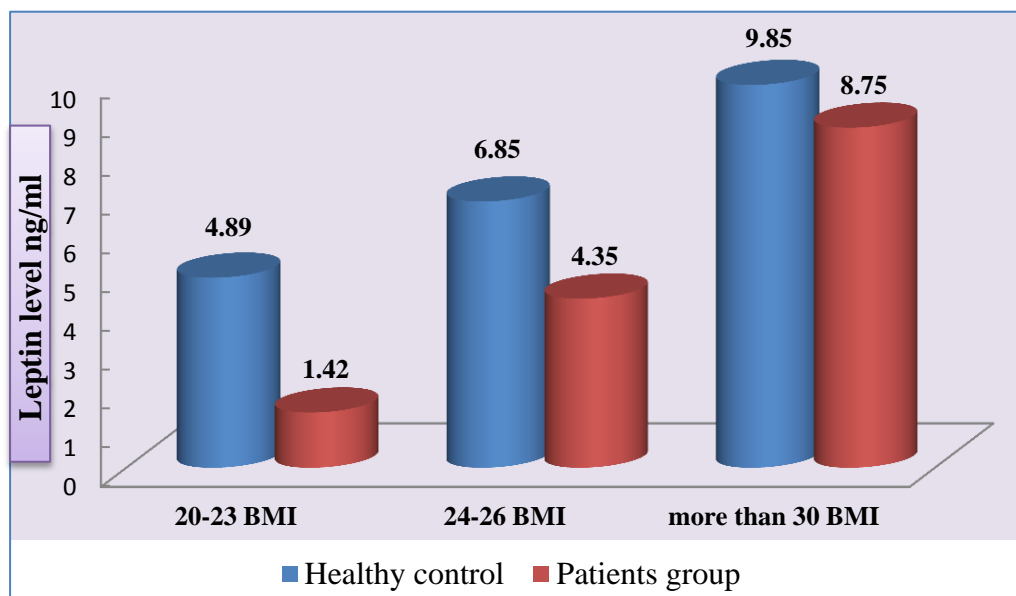


Fig. 1: Comparison between healthy control and patients group for leptin level according to BMI.

Leptin is produced in adipose tissue and it has an effect in inhibiting energy intake, so the decrease in secretion of leptin may represent a mechanism of compensatory when there is imbalance in energy [20]. In another study, there was a decrease in leptin level between the groups of patients with lung cancer compared to the healthy control, and the study showed that the decrease level of leptin in lung cancer patients with weight loss is due to decreased production of leptin in advanced stages of cancer due to low fat mass caused by the case of cachexia which is a condition of loss of appetite, weight loss and muscle atrophy [21]. Evidence suggest a role for leptin in the development of cancer at least partially by its up-regulatory function in the inflammatory system, and leptin involves in the immunity by stimulating blood mononuclear cells, neutrophils, T-cell, macrophages, and dendritic cells, in turn the products of these cells may induce chronic inflammation and lung carcinoma [22].

In this study the results also showed that leptin level significantly associated with BMI in patients with lung cancer, leptin is associated with obesity as it rises in obese people and when a loss of body weight occurs, the level of leptin decreases. In another study the results showed the increased of leptin level in obese persons is linked with the large amounts of fatty

tissue, which influence the immune system and contribute to cancer [23]. Evidence has shown that leptin is associated with tumourigenesis and the spread of cancer to other organs [24], and leptin plays a significant role in the initiating and advancing of cancer [25]. The results have also been shown that there was an increase in ALT activity of lung cancer patients compared to healthy control, while there was no significant decrease in AST activity compared to healthy control as shown in [Table 2](#).

These enzymatic changes may be caused by the spread of cancer cells to the liver, which is called liver metastasis, and studies have shown that 25-50% of patients with cancer have been observed liver metastasis, as the cancer is usually spread to the liver because it provides a suitable condition for the proliferation of cancer cells because of the dual blood supply [26], and these significant differences in the ALT activity may be due to the abundance of this enzyme in the liver and in trace amounts in the lungs and other organs [27], While AST is excreted in large amounts in the heart compared to other organs of the body such as liver and kidneys [28].

As shown in [Table 3](#), there was an inverse but statistically not significant correlation between leptin and ALT activity in patients group ($r = -0.104$, $p = 0.477$) and the correlation was direct but statistically not significant between leptin and AST activity ($r = 0.092$, $p = 0.525$).

Table 1: Leptin levels in the studied groups according to BMI.

Body mass index	Leptin levels (ng/ml)		
	Healthy control	Patients group	p-value
20 – 23 kg/m ²	4.89 ± 1.29	1.42 ± 0.54	0.010
24 – 26 kg/m ²	6.85 ± 1.49	4.35 ± 2.19	0.045
more than 30 kg/m ²	9.85 ± 2.62	8.75 ± 1.2	0.07

* ($P \leq 0.05$) = significant.

Table 2: ALT and AST activity in the studied groups.

Parameters	Healthy control	Patients group	p-value
ALT (U/L)	22.8 ± 6.55	30.8 ± 16.4	0.018
AST (U/L)	27 ± 9.2	25.4 ± 8.9	0.06

* ($P \leq 0.05$) = significant.

Table 3: The correlation between leptin and ALT, AST activity in the patients group.

Parameters	Correlation (r)	p-value
Leptin & ALT	-0.104	0.477
Leptin & AST	0.092	0.525

4. Conclusions:

Levels of leptin were decreased in patients with lung cancer compared to healthy control which may be the result of a compensatory mechanism during an energy imbalance in the body of patients and also there was a relationship between leptin and BMI. The study also showed the effect of lung cancer on some liver function enzymes which may be due to the process of metastasis. The results revealed no correlation between the level of leptin and the liver enzymes activity (ALT, AST).

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