

**Evaluation of Tumor necrosis factor-TNF  $\alpha$  and some vitamin levels and ferritin in women with Breast Cancer in Kirkuk City**

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## Evaluation of Tumor necrosis factor-TNF $\alpha$ and some vitamin levels and ferritin in women with Breast Cancer in Kirkuk City

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### Abstract

This study aimed to evaluate the role of Vitamin D3 deficiency in women with breast cancer. This study was conducted to estimate tumor necrosis factor (TNF)-  $\alpha$  and vitamins (D3, B12, folate), and ferritin levels this study estimate. Some hematological parameters such as hemoglobin (Hb), white blood cells (WBC), platelet level, erythrocyte sedimentation rate (ESR) in women with breast cancer patients. The study started from november 2022 to march 2023, The study population included 50 females, with them 15 in the healthy control (control group) and 35 patients with breast cancer (patient group), whose ages ranged from 25 to 96 years also the mean age is 53 years.

The current study showed a significant low ( $P < 0.05$ ) in the mean vitamin D3 level ( $25.97 \pm 13.5$  ng/ml), vitamin B12 ( $288.63 \pm 78$  pg/ml), folate ( $9.44 \pm 4.6$  ng/ml), hemoglobin level ( $11 \pm 1.52$  g/L), and percentage of packed cell volume ( $31 \pm 10.6$ ) in the patient group with the control group. Also, the current study shows elevated ( $P < 0.05$ ) in the TNF  $\alpha$  and the mean of white blood cells ( $20 \times 10^9 \pm 24.5$  cell/mm<sup>3</sup>) and Platelet level ( $269 \pm 143.8$  billion/L) and ESR ( $203 \pm 11.3$  mm/hr) and ferritin level ( $157.4 \pm 113.4$  ng/ml) in the patient group among to the control group.

**Key words: - Breast cancer, Tumor necrosis factor, Vitamins, Ferritin .**

### Introduction:

Breast cancer is one of the most common malignant types of tumors<sup>(1,2,3)</sup>. It's incidence is higher in women than men<sup>(4,5)</sup>. It is a disease that has a genetic background but environmental factors donate to it' occurrence and shows a large degree of heterogeneity between and within tumors<sup>(6,7,8)</sup>. Tumor necrosis factor (TNF)- $\alpha$  is one of the cytokines that are secreted from macrophages and natural killer cells. This cytokine promotes inflammation. It is contribute to development of cancer<sup>(9)</sup>. TNF is used as a tumor marker to determine the stage of breast cancer<sup>(10)</sup>, and that its mechanism of action is through receptors on the cell surface to regulate the programmed cell death pathway<sup>(11)</sup>. Vit.D3 is a known has potential anticarcinogenic impacts, including regulation of cell growth and proliferation, stimulation of apoptosis, and down-regulation of estrogen receptors<sup>(12, 13)</sup>. Ferritin is protein mainly

synthesized in the liver (14). Recently, there is an evidence that ferritin has a role of in the pathogenesis of a number of diseases, including breast cancer (15).

**Materials and methods:**

**Study design:**

Fifty blood samples were collected, 35 samples from women with breast cancer, and 15 samples from control group whose ages ranged between (25-96) years. After that, the blood was separated and preserved until tests were conducted.

**-Estimation of complete blood count (CBC) levels in the blood:**

The level of CBC was evaluated according to a kit manufactured by the company Starlab.

**-Estimation of Tumor necrosis factor levels in the blood serum:**

The level of tumor necrosis factor was estimated according to a kit prepared by the company Starlab.

**-Estimation of Vit. D3, B12 and folic acid level in the blood serum:**

The level of vitamins (D3, B12, and folic acid) was estimated according to a kit organized by the company Nepegon health crop.

**-Estimation of ferritin level in the blood serum:**

The level of ferritin was evaluated according to a kit prepared by the company Nepegon health crop.

**Statistical analysis:**

The result analyzed using the statistical package for the social science (SPSS) program. Descriptive statistics like mean, frequency, and percentage were conducted. Other inferential statistical test like unpaired T-test was employed for assessing relation between TNF- $\alpha$  levels and breast cancer. The differences were taken as statistically significant when  $P < 0.05$ .

**Result and Dissection:**

Hematological parameters:

The blood from participants (patient and control) was tested for hemoglobin Hb, packed cell volume (PCV), Platelets (PLT), and ESR, and the results shown in Table 1

Table 1 shows the mean  $\pm$  standard deviation (SD) of hematological parameters in control group and patient group.

Variables	Control group	Patient group	P value t- test
	Mean $\pm$ SD	Mean $\pm$ SD	
Hb ( g/L )	14.4 $\pm$ 1.8	11 $\pm$ 1.52	1.95 *
PCV ( % )	39.6 $\pm$ 4.57	31 $\pm$ 10.6	0.32
WBC ( cell/mm <sup>3</sup> )	7.5 $\times$ 10 <sup>9</sup> $\pm$ 2.3	20 $\times$ 10 <sup>9</sup> $\pm$ 2.56	0.15
PLT ( billion/L)	254.3 $\pm$ 88.8	269 $\pm$ 143.8	0.021
ESR ( mm/hr )	8.7 $\pm$ 5.3	203 $\pm$ 11.3	0.22

Figures (1, 2, 3, 4 and 5) demonstrated a significant reduce in the level of Hb, PCV in the patinas compered control group. Also the results showed the increase in the mean of platelet and ESR for the patient compared to the control group.

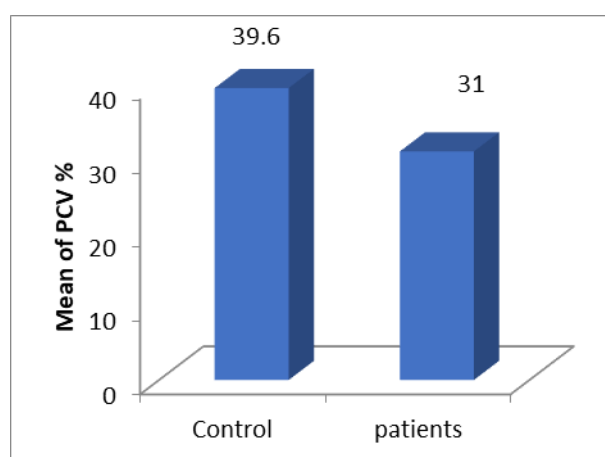


Figure 2: The level of PCV in blood group.

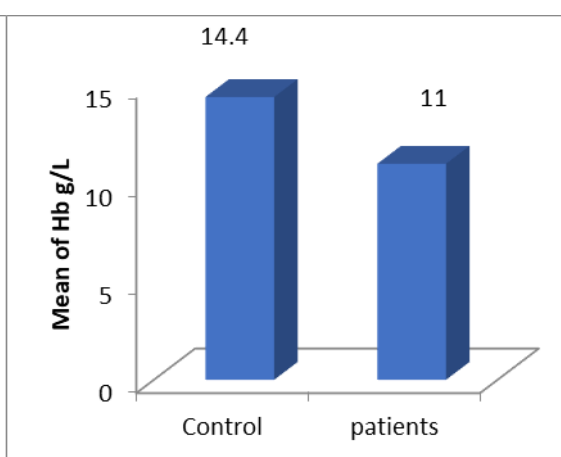


Figure 1: The level of Hb in blood group.

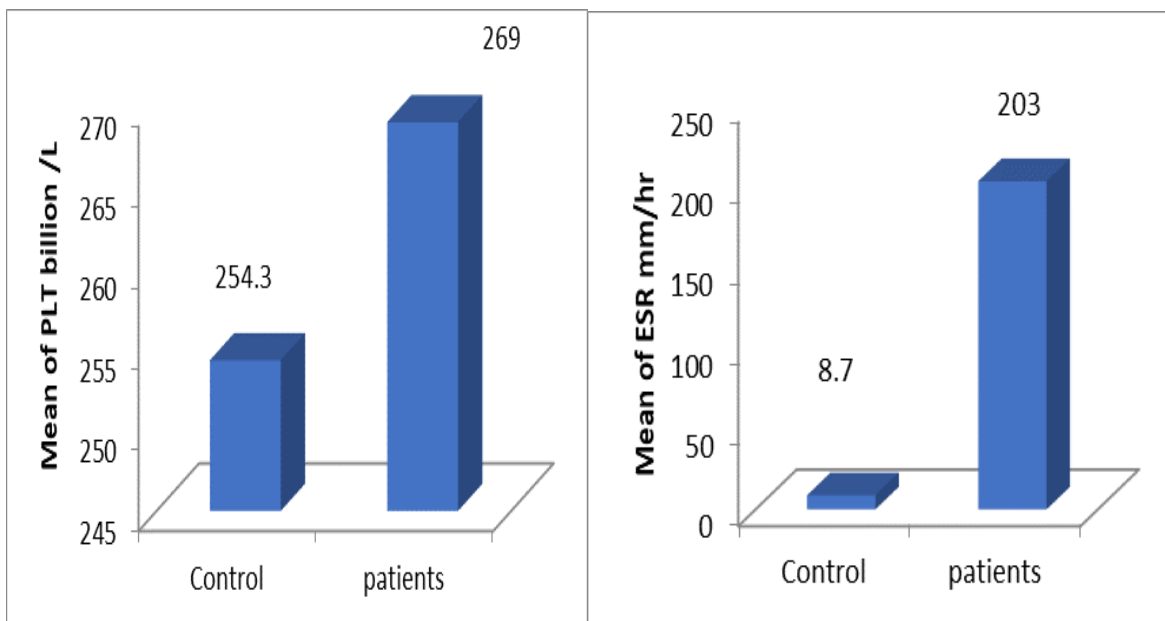


Figure 4: The level of PTL in blood group.

Figure 3: The level of ESR in blood group.

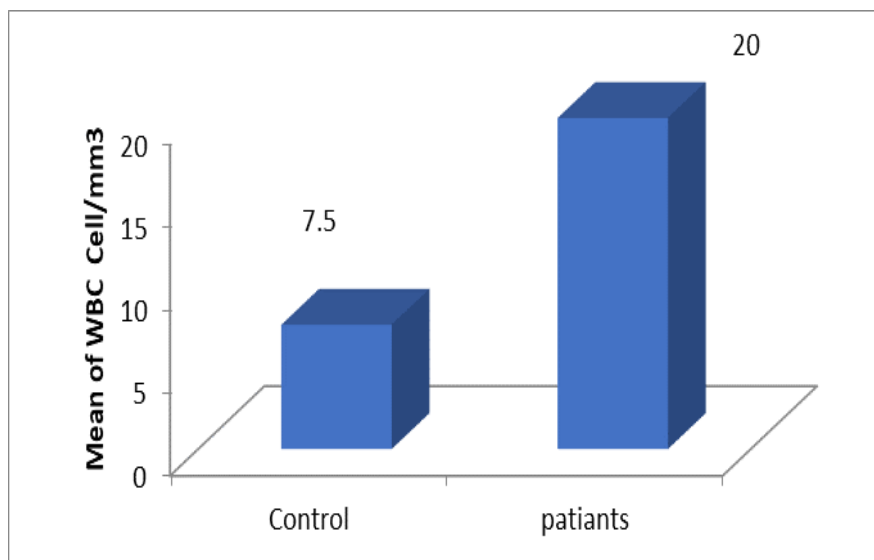


Figure 5: The level of WBC in blood group.

Estimation of tumor necrosis factor and Vitamin D3, Vitamin B12, Folate, and Ferritin level:

Table 2 shows the mean  $\pm$  SD of biochemical parameters in control group and patient group.

Parameters	Control group	Patient group	P value t - test
	Mean $\pm$ SD	Mean $\pm$ SD	
TNF- $\alpha$ (ng/ml)	55.312 $\pm$ 10.421	130.212 $\pm$ 20.421	1.7*
Vitamin D ( ng/ml )	31.6 $\pm$ 13.9	25.97 $\pm$ 13.5	1.7*
Vitamin B12 ( pg/ml)	316.5 $\pm$ 82.3	288.63 $\pm$ 78	0.038
Folate ( ng/ml )	11.7 $\pm$ 4.6	9.44 $\pm$ 4.6	0.8
Ferritin ( ng/ml )	144.6 $\pm$ 68	157.43 $\pm$ 113.4	0.028

The result showed a significantly increase in TNF- $\alpha$  and ferritin levels in breast cancer patients compared to controls as in figure (6,7) , also the results showed a significantly decline in all vitamins ( D3, B12 and folic acid) in breast cancer patients compared to controls as in figure (8,9, 10) .

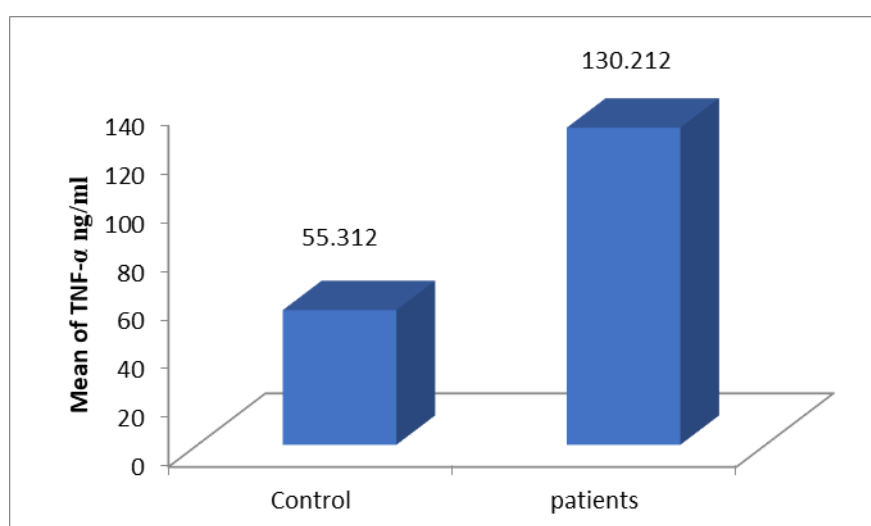


Figure 6: TNF- $\alpha$  level in blood serum

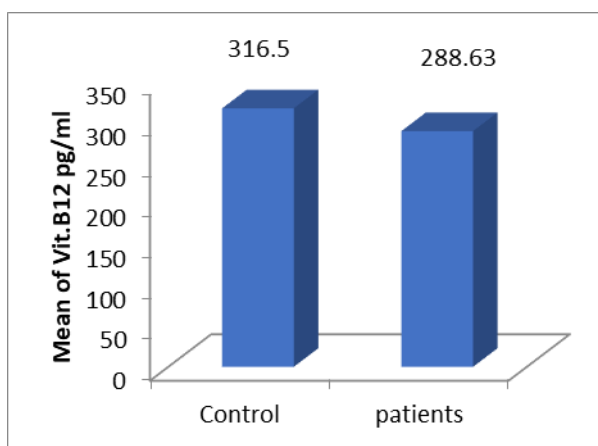


Figure 8: Vit.B12 level in blood serum

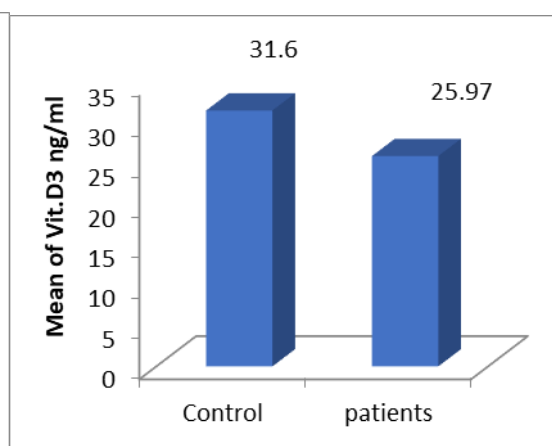


Figure 7: Vit.D3 level in blood serum.

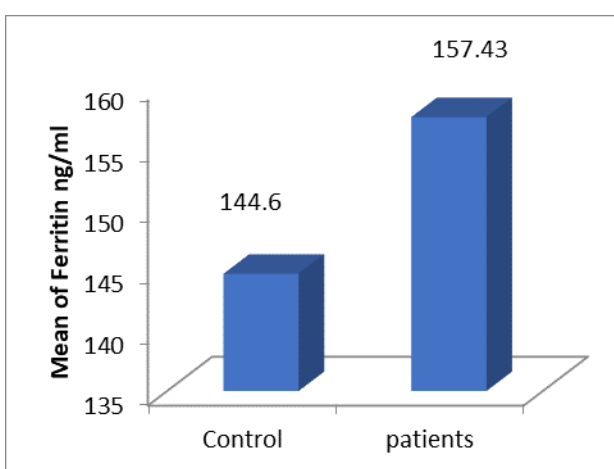


Figure10: Ferritin level in blood serum.

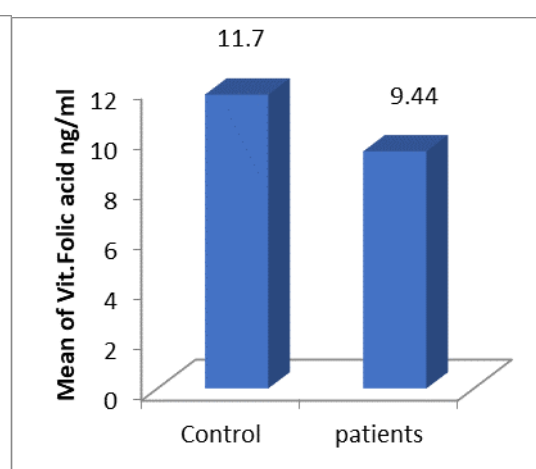


Fig 9: Folic acid level in blood serum.

The result displayed that the bleeding occurring and related to the tumor's invasion of the bone marrow may be lead to low level of Hb rate and the PCV percentage, the consequence is the bone marrow failure<sup>(16)</sup>. Alternatively, white blood cells have been found to be associated to breast cancer<sup>(17)</sup>. Cancer cells causes thrombocytosis and platelet aggregation that are the reasons for high platelets<sup>(16)</sup>. On the other hand, it was found that the cancer has relationship with increased level of erythrocyte sedimentation ratte<sup>(18)</sup>.

TNF-blockers act as therapeutic agents in solid tumors, but patients with elevated in TNF- $\alpha$  fail to respond to infliximab, due to consumption of circulating TNF-blockers and tumor progression<sup>(19)</sup>. TNF activates nuclear factor Kappa (NFK) B<sup>(19)</sup>. TNF when exposed to cancer cells<sup>(20)</sup>, as NKB-TNF plays an important role in inflammation, immune regulation, cell differentiation, and tumor formation<sup>(21)</sup>, and contributes to cancer cell proliferation, tumor angiogenesis in cancer cells, stimulation of cell proliferation and prevention of apoptosis<sup>(22)</sup>. One of the TNF receptors TNF- $\alpha$  that is located inside the mitochondria and has relationship with apoptosis<sup>(23,24)</sup>. Vitamin D deficiency is highly valuable

consequence of breast cancer in women <sup>(25)</sup>. The low level of serum folate and vitamin B12 is considered indicator for improved breast cancer risk <sup>(26)</sup>,

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