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Study of the effect of cancer antigen CA15-3 and CRP on Liver enzymes and Kidney function in patients with breast cancer in Al-Muthanna Governorate

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Abstract
This study was conducted in the laboratories of Al-Hussein Teaching Hospital and some private laboratories in the city of Samawah in Al-Muthanna Governorate for a period from 1/15/2024 to 3/15/2024. The study included (80) samples of women of reproductive age, ranging in age from (25-70). year, and were divided into two groups:
• **Patient group:** (40) samples of patients with breast cancer.
• **Control group:** (40) samples of healthy women.
The pathological cases of women with breast cancer were confirmed after conducting clinical examinations and referring them to the specialist doctor and performing an ultrasound examination. After that, blood was taken from both groups (patients and healthy people) and separated using a centrifuge. Then the level of cancer antigen was measured. CA15-3 and CRP to confirm whether they have breast cancer, in addition to measuring immune and physiological variables. The results of the current study showed a significant increase in each of the diagnostic indicators, liver enzymes, and kidney functions in the blood serum of both groups, at a level of probability $P \leq 0.05$.

Key words : Breast cancer, CA15-3, CRP, Liver enzymes, Kidney function.

Introduction

Cancer is known as a disease that spreads rapidly in the body. It is an uncontrolled disease that has the ability to grow and spread very quickly, unlimited fission of the body's various cells, and the ability of its cells to attack nearby body tissues and destroy them. Destroy, or move through the blood to distant body tissues. This is called It is characterized by a malignant tumor. There is another type of cancer that is characterized by specific growth and its inability to metastasize and attack various cells in the body. It is called a benign tumor. This type can develop in the body and divide into several divisions, ultimately leading to malignant cancer [(1).]

Breast cancer is considered the most common type of cancer that causes death among women, as surgical resection is a major treatment method, and local recurrence of the tumor plays an important role in the overall oncological outcomes with regard to survival for each type of cancer [(2).] So more than half of cancer cases In Iraq, it is in the breast [(3)], as it was found in Iraq that breast cancer is the first malignant tumor that affects society and is the main cause of cancer-related deaths among Iraqi women and the second main cause in general among men and women after bronchogenic cancer [(4)].

Breast cancer spreads from one part to another and from one site to another in different parts of the body, that is, it is considered a metastatic disease, and its symptoms vary according to the site to which the tumor moves in the body. Among these common sites to which breast cancer spreads are the brain, liver, lungs, and bone [(5).] in addition to the indicators that indicate the presence of metastatic breast cancer are sudden weight loss, joint pain and bone breakdown, high temperature and yellowing, i.e. jaundice, and various other neurological symptoms [(6).] The methods of diagnosing breast cancer depend on several diagnostic parameters, including the clinical examination first, physical tests second, and computed tomography third, in addition to the use of ultrasound and laboratory tests. Among these laboratory tests are measuring the level of tumor markers (Tumor marker) and measuring the level of cancer antigen CA15-3. In addition to measuring the Human 2 Epidermal Growth Factor receptor (HER2), as well as measuring the CRP level, these examinations and tests provide the treating physician with predictions, diagnostic probabilities, and complete information to begin the treatment phase for patients with breast cancer [(7).]Cancer antigen CA15-3 is one of the naturally produced proteins found in breast tissue in the human body,The level of this cancer antigen increases in the presence of cancerous tumors, especially breast cancer [(8).] The level of the cancer antigen CA15-3 increases in the case of metastatic breast cancer, pancreatic, lung, and rectal cancer, in addition to liver cancer, and it may also increase in some benign tumors in the breast and liver. CA 15-3 increases in less than 33% of patients with breast cancer of stages II and I[(9).] The level of carcino antigen CA15-3 increases in patients with cancer by more than 79-92%, especially advanced breast cancer, as the use of this antigen is very useful to know the pathological stage that breast cancer has reached in order to begin treatment, as its decrease is slight in relation to For successful treatment, therefore, a period of investigation is required to confirm the significant decrease in CA15-3 [(10)] The kidney is the main organ in maintaining homeostasis within the body by controlling the amount of fluids, neutralizing salts, and ridding the blood of metabolic wastes. The kidney's functions are not limited to filtering the blood and converting wastes into urine, but go beyond that to other functions, the most important of which is maintaining the pH balance. In the body, regulating blood pressure, and producing hormones that affect bones and blood [(11, 12).]Kidney functions have many variables, including urea, creatinine, and uric acid. It was found that urea nitrogen in the blood and creatinine are the final products of nitrogen metabolism in the human body, as each of them is filtered from

the body by the nephrons due to their small size, where they are easily carried out. In addition, they are filtered from the body by the nephrons. Urea reabsorbs at least 30% to 40% of the tubules [13,14].

As for liver enzymes, they include (AST), which is found in high concentrations in cardiac muscles, skeletal muscles, liver, kidneys, and red blood cells [15]. This enzyme is also found in the liver's mitochondria. The presence of an analogue of this enzyme in the cytoplasm is also found in the mitochondria, where it is associated with wound conditions. The light that occurs in tissues, and the most obvious form of the enzyme in serum is from the cytoplasm, where large amounts of the enzyme are released into mitochondria as a result of tissue breakdown [16]. Liver enzyme levels (AST and ALT) are a valuable and effective aid in diagnosing liver diseases. We can also use these enzymes to monitor the course of liver disorders in various diseases of the body. In addition, the amount of AST and ALT in the blood is directly related to the extent of liver damage or tissue damage. In addition, the AST/ALT ratio can help us determine whether the liver is damaged or another organ has been damaged [18,17]. Through the increase in diagnostic indicators, the current research aims to study the effect of the cancer antigen CA15-3 and CRP with liver enzymes and kidney function in patients with breast cancer in Al-Muthanna Governorate.

Collection of specimens

This study was conducted in the laboratories of Al-Hussein Teaching Hospital and some private laboratories in the city of Samawah in Al-Muthanna Governorate for a period from 1/15/2024 to 3/15/2024. The study included (80) samples of women of reproductive age, ranging in age from (25-70). year, and were divided into two groups:

- **Patient group:** (40) samples of patients with breast cancer.
- **Control group:** It was (40) samples of healthy women

The pathological cases of women with breast cancer were confirmed after conducting clinical examinations and referring them to the specialist doctor and performing an ultrasound examination. After that, blood was taken from both groups (patients and healthy people) and separated using a centrifuge. Then, diagnostic indicators, liver enzymes, and kidney function were measured. The results of the current research showed a significant increase in each of the diagnostic indicators, liver enzymes, and kidney function in the blood serum of both groups, at the level of probability $P \leq 0.05$.

- **Estimating levels of diagnostic indicators in blood serum:**

The level of the hormone (cancer antigen CA15-3 and CRP) was estimated using the ELISA technique (Sandwich), where the antibodies to the cancer antigen CA15-3 and CRP were pre-fixed in the holes of the microtiter plate. The blood serum of the samples is added to the holes of the plate to bind to the cancer antigen CA15-3. 3 and CRP in the sample with antibodies treated with biotin and coated the holes, after which their Streptavidin-HRP is added to each well in succession and incubated, the pits are then washed with wash buffer to remove unbound antibodies. The matrix solution is then added so that the color develops in proportion to the level of cancer antigen CA15-3 and CRP in the serum, The reaction stops after adding the acidic Stop solution to it. The absorbance of each pit is then read at Wavelength 4500.

- **Estimating the levels of physiological indicators in blood serum:**

The concentration of each level (Urea, Creatinine, AST, ALT) was measured by adopting the ELISA technique (Sandwich) and by following the ready-made steps indicated in the custom analysis kit, and it differs from one device to another and according to its manufacturer.

Statistical Analysis

The process of collecting data for the samples used for the study and analyzing them statistically was done using the SPSS system by extracting the arithmetic mean and standard deviation. The test was also used to analyze the differences between the group of patients and healthy people. Significant differences were chosen for these groups under a probability level of $P \leq 0.05$

Result and Desiccation

- Measuring the levels of diagnostic, immunological and physiological indicators in a group (patients and healthy people):

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Table No. (1) shows the mean ± standard deviation of the diagnostic indicators, liver enzymes, and kidney functions in the samples under study

Groups / Parameter	Mean ± SD		P-Value
	Control n=40	Patients n=40	
CA15-3 (U/ml)	5.18±0.87	50.68±17.91	P≤0.05
CRP (ng/ml)	10.79±1.67	5.95±0.67	P≤0.05
AST(IU/L)	23.21±3.44	30.73±3.43	P≤0.05
ALT (IU/L)	21.89±3.15	32.17±2.96	P≤0.05
Urea (mg/dl)	14.24±0.51	30.74±0.62	P≤0.05
Creatinine (mg/dl)	0.41± 0.089	0.79±0.049	P≤0.05

The results of the current study for patients with breast cancer compared to healthy women showed a significant increase in each of the diagnostic, liver enzymes, and kidney function in the serum of both groups (patients and healthy people), at a probability level of $P \leq 0.05$. As in the following figures.

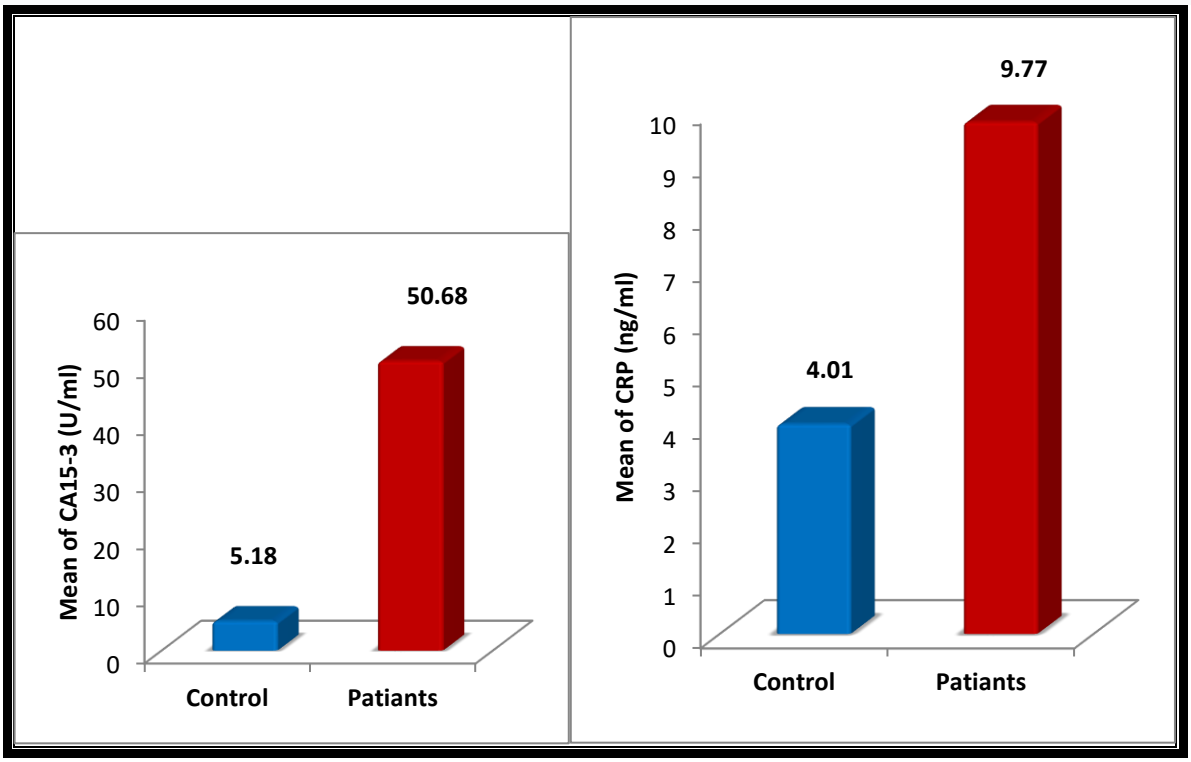

Figure (1) : CA15-3 in the blood sera of the samples under study

Figure (2) : CRP in the blood sera of the samples under study

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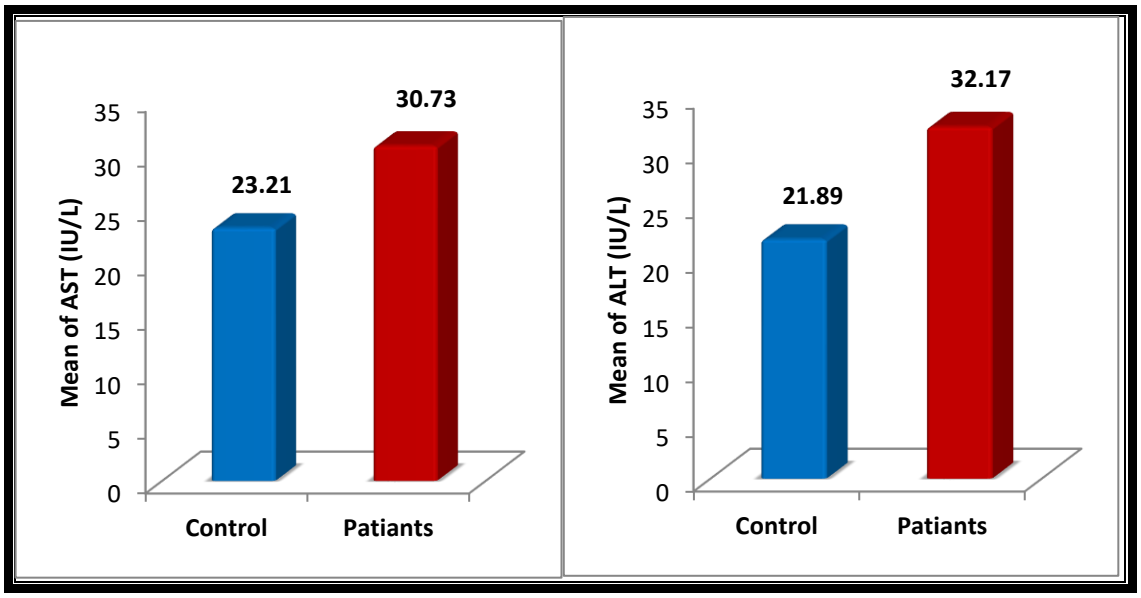

Figure (5) : AST in the blood sera of the samples under study **Figure (6) : ALT in the blood sera of the samples under study**

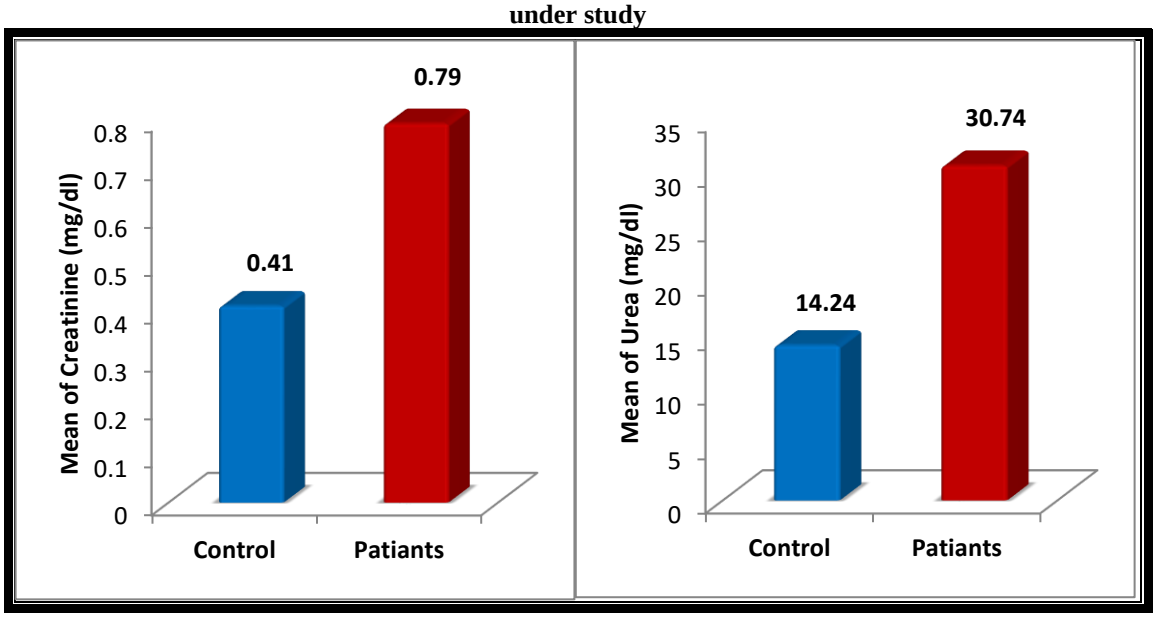

Figure (5) : Urea in the blood sera of the samples under study **Figure (6) : Creatinine in the blood sera of the samples under study**

Desiccation

Cancer antigen (CA15-3) and CRP are considered one of the diagnostic markers that help treating doctors in early diagnosis of breast cancer, starting the stage of treating patients, and assessing important predictive factors for them. One study showed that levels of cancer antigen (CA15-3) and CRP increase significantly in patients with breast cancer. Patients with breast cancer and cancerous tumors [19].

The significant increase in the level of cancer antigen (CA15-3) led to the results of his study being consistent with the results of the study of Hamdi and his group [20] and the results of the study of Feng and his group [21], who indicated in their study that the cancer antigen CA15-3 is significantly high in Women with breast cancer, which indicates that there is a chance for the disease to develop or spread to other organs of the body, as the CA15-3 test is the main predictor of diagnosing cancers in the body, including breast cancer, and when a change occurs in the level of CA15-3, these changes are reflected in the stage of the disease if markers are used. Tumor in clinical practice, Therefore, this will lead to giving the appropriate treatment to indicate its effect on the body. Therefore, CA15-3 is the most useful diagnostic marker with high specificity, moderate sensitivity, and suitable for predicting long-term malignant tumors that occur in the body. Therefore, most studies indicated that CA15-3 is considered a diagnostic marker. Important for patients with breast cancer and other cancers [22,23].

As for the other diagnostic indicator, it is CRP, as the results obtained are consistent with the findings of Panis et al [24], Allin et al [25], and Celik et al [26], who indicated in their study an increase in the level of CRP in patients with breast cancer compared to the control group. The reason for the increase in the concentration of CRP in the serum of women with breast cancer is due to chronic inflammation, which is one of the main factors that contribute to the development and progression of the carcinogenesis process, as inflammatory pathways play an important role in causing breast cancer. C-reactive protein is an inflammatory protein that interacts in the acute phase. It is synthesized in liver cells in response to cytokines that are released from leukocytes within the tumor microenvironment. Thus, CRP concentrations in the blood circulation increase in response to acute inflammation [27], and it has prognostic value in breast cancer patients [28].

An increase in the level of the AST enzyme in the body is not an indicator of liver disease only. When a breast tumor or liver damage occurs, it can cause a noticeable increase in the level of the AST enzyme [29]. This enzyme sometimes causes an increase in the effectiveness of liver enzymes in patients with breast cancer during the period Follow up on the therapeutic phase. This effect may sometimes be associated with the name non-alcoholic fatty liver disease, known as the malignant tumor itself that is caused by medications, chemotherapy, or some other known risk factors that may cause fatty degeneration, We found that the AST/ALT effectiveness ratio has no effect on the rate of fatty liver degeneration in the body, but AST may be a natural variable more easily in patients suffering from some types of cancer, especially breast cancer [30]. The results of our current study are consistent with the findings of researcher Ashtee A and his group [31], who showed in his study an increase in the level of AST in breast cancer patients.

As for the level of ALT, its results agreed with the findings of M. Korangath et al [32], as the increase in the activity of the ALT enzyme in breast cancer patients is linked to many cancer cell lines that have high expression in the activity of ALT, whether in the mRNA or protein that caused it. In addition, factors Current adjuvant chemotherapy doxorubicin, cyclophosphamide, and paclitaxel have a significant and effective role in the treatment of breast cancer patients, and are less hepatotoxic than the chemotherapy regimen including methotrexate used in its treatment.

As for the level of kidney function, the results of patients with breast cancer agree with the results of AL-Hussein [33], and Chauhan and his group [34], whose results showed that there was a noticeable significant increase in urea concentrations in the blood serums of both groups (patients and healthy people), and that the urea level is... It is an important chemical diagnostic parameter for monitoring cancerous diseases, especially breast cancer. While another study showed that its results did not agree with the results of our study, which indicated that there was no difference in urea concentrations when comparing women with breast cancer, as they were within the normal range [35],In addition, the results of another study showed a non-significant and slight increase in urea concentration in the group with breast cancer compared to healthy people [36].

Breast cancer patients often suffer from swelling in the chest area and previous comorbidities that increase the possibility of kidney failure or decline before receiving the necessary treatments that are likely to be toxic and harmful to the kidneys [37]. As most of the chronic kidney disease is in elderly and advanced people [38].

As for the Creatinine level, it is considered the second parameter with high sensitivity to kidney function in the human body and has an important role in monitoring cancer patients. The results of our current research are consistent with the results of the research of Chauhan and his group [34], who showed in their study that creatinine levels are normal in patients with breast cancer. Compared with the control group, the reason for the lack of difference between creatine levels is due to Organic Cation Transporter 2 (OCT2), which plays an important and effective role in the secretion of creatinine from the kidneys, as the basic substances present in OCT2 can work to reduce renal creatinine secretion, which indicates a defect. In the work of the kidneys in the body [39]. Therefore, the human organic cation transporter OCT2 plays an important role in the renal excretion of cationic compounds in the body, as the tissue expression and membrane localization of OCT2 are closely related to its tissue distribution in the body [40].

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