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Serum Alkaline Phosphatase, Iron and Calcium Levels in Breast Cancer and Leukemia Patients in Salah Al-Din Province

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ABSTRACT:-

This study was conducted on 19 breast cancer and 23 leukemia patients with ages ranged between 25-70 years old registered in Tikrit teaching hospital, Tikrit city, with the fifty four normal subject's volunteers and age ranged between 30-60 years old. Statistical analysis, show there were highly significant differences ($p<0.05$) between the mean levels of calcium, iron and alkaline phosphatase in breast cancer and leukemia compared with the normal subjects. We found that the mean levels of serum calcium were higher in leukemia than in breast cancer and normal subjects, also we found higher mean values of serum iron in breast cancer compared with the leukemia and healthy subjects. The activity of the ALP was found elevated in both patients and increased levels of ALP depends on the concentration of serum iron. . We done this study to show effect of the age on calcium, iron and ALP levels in breast cancer and leukemia.

دراسة مستوى انزيم الفوسفاتيز القاعدي ،الكالسيوم والحديد في مصل الدم عند مرضى سرطان الثدي وابيضاض الدم في مدينة صلاح الدين

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المستخلص:-

تضمن البحث تقدير فعالية انزيم الفوسفاتيز القاعدي وبعض العناصر المعدنية منها الكالسيوم والحديد لدى مرضى سرطان الثدي وابيضاض الدم ومقارنتها مع مجموعة السيطرة الاصحاء. وقد بين التحليل الاحصائي بأن هناك فروقات معنوية عند مستوى احتمالية ($p<0.05$) بين متوسطات قيم العناصر والانزيم لدى مرضى السرطان والاصحاء وتدرج هذه الاختلاف بين نوعي السرطان حيث وجد ان تركيز الكالسيوم في مصل مرضى ابيضاض الدم يرتفع ارتفاع عالي مقارنة مع القيم المقاسة في سرطان الثدي ومجموعة السيطرة على العكس وجد ان تركيز الحديد في مرضى سرطان الثدي يزيد ارتفاعاً ملحوظاً يصل الى الضعف بالمقارنة على ما هو عليه في مرضى ابيضاض الدم والسيطرة. اما بالنسبة الى فعالية انزيم الفوسفاتيز القاعدي لوحظ ارتفاع معنوي عند مستوى احتمالية ($p<0.05$) وهذا الارتفاع مرتبط بارتفاع تركيز الحديد . تم جمع العينات من مستشفى تكريت التعليمي ولاعمار مختلفة تراوح بين(25-70) سنة. اذ درس تأثير العمر على مستويات الانزيم والكالسيوم والحديد حيث وجد ان هنالك فروقات معنوية عالية عند مستوى احتمالية ($p<0.05$) في فعالية الانزيم والعناصر المعدنية لدى مرضى سرطان الثدي وابيضاض الدم بالمقارنة مع السيطرة الاصحاء.

INTRODUCTION:-

Alkaline phosphatase (ALP; EC 3.1.3.1) comprises a group of enzymes that catalyze the hydrolysis of phosphate esters in an alkaline environment, generating an organic radical and inorganic phosphate (1). Like other enzymes, this enzyme has many isoenzymes. In healthy adults, these enzymes are widely distributed in nature, including prokaryotes and higher eukaryotes; this enzyme is mainly derived from the liver, bones and in lesser amounts from intestines, placenta, kidneys and leukocytes (2). In healthy adults, most of the alkaline phosphatase (ALP) activity in serum is derived from liver ALP and bone ALP, also this enzyme present in mammary gland*(3)*. In humans, at least four distinct classes of this enzyme have been identified using genetic and biochemical analysis (2, 3). An increase in serum ALP levels is frequently associated with a variety of diseases. Such disorders as extrahepatic bile obstruction, intrahepatic cholestasis, infiltrative liver disease and hepatitis are mentioned. Unfortunately, the elevation of ALP less than three times the normal level is considered non specific and insufficient to provide a definite diagnosis (4). Markedly elevated serum ALP, hyper alkaline phosphatasemia, is seen predominantly with more specific disorders, including, malignant biliary obstruction,

primary biliary cirrhosis, primary sclerosing cholangitis, hepatic lymphoma and sarcoidosis (5). Increasing level of ALP may be due to physiological changes in the body and these changes result from diseases in liver or bone, increased iron binding protein level and low level of protein (albumin) as a result from disorder in acid base balance (6). The trace elements is present in low concentration but it plays an important roles, some of them act as cofactor and others enter in structure of enzyme molecule like phosphatase enzymes, calcium enter in ALP molecule structure (1), so this study include the relation between ALP and trace elements and to show effect of trace element and their relation with the cancer, and the study of the etiologies of high serum ALP can be useful data in diagnosis. Previous studies show differences in zinc and iron levels in acute lymphatic lecukemia patients (7), and Rosas et al shows differences in level of iron and calcium in breast cancer patients (8) so the aim of current study is to show levels of ALP and some elements in serum of leuckemia and breast cancer patients in salah Al- Din population.

MATERIALS AND METHODS:-

1. Normal and cancer subjects: This study was conducted on 19 breast cancer and 23 leukemia patients with ages ranged between 25-70 years old registered in Tikrit teaching hospital, Tikrit city, with the fifty four normal subjects' volunteers and age ranged between 30-60 years old at the same experimental studying period and from the same region. Age group in both normal and patients were Mean of serum levels in group 3 aged ranged (55-70) was higher than other group in patients Table (3) showed the distribution of serum Alkaline Phoshatse in patients and normal subjects in relation to the age. And the mean serum ALP levels in three groups of age was significantly ($p< o.oo5$) higher than mean levels in normal subjects. And the mean levels of ALP in group 2 of age ranged (50-55) was higher than other groups. To the age ranged from 25-70 yrs old. In three groups of age, the level of calcium mean conc. of breast cancer and leuckemia was significantly ($p< o.oo5$) higher than the mean of calcium levels in normal individuals. Table (2) showed the distribution of serum iron of both normal and patients and iron levels in relation to age. Were in age groups 1, 2, 3. . mean serum iron values in both patients was significantly ($p< o.oo5$) higher than normal subjects and the mechanism of hypercalcemia was unclear and was attributed to increased osteoclastic activity or transformation of the CLL to prolymphocytic leukemia (15) Table (2) showed serum iron levels were significantly ($p<0.05$) higher than in patients of both breast cancer and leukemia compared with the normal subjects. Also we showed high mean of serum iron levels within the 1st and 3rd group of age in leukemia patients compared

divided into three groups: group 1 (25-50 yrs), group 2 (50-55 yrs), group 3 (55-70yrs). Using cresolphthalein complexone method (10). It was expressed as mg/100 ml. Serum iron level was measured by using serum iron kit (Sybrio) Bathophenanthroline method (11). It was expressed as µg/100ml. Statistical analysis Student's *t* tests were performed in the statistical package computer program for social sciences (Spss computer program). All results are expressed in the form of mean values ± standard deviation (SD), with statistical significance differences at probability less than 5%, ($P < 0.05$).

RESULTS:-

Table (1) showed the distribution of serum calcium mean conc. mg/dl of both normal and breast, leuckemic patients in relation.

2. Blood-samples: At the morning about 5ml of venous blood was drawn from capital vein using disposable needle and syringe, collected blood, was put in clean dry plastic tube and was allowed to clot at 37C for 25 minutes, and blood samples were centrifuged at 3000 rpm for 15 minutes. It was essential to ensure that the serum did not show haemolysis. Serum obtained was used for the determination of serum ALP, calcium and iron.

3- Serum Alkaline phophatase: Serum ALP was measured by using kit (ALk-Ph) (9). It was expressed as U/L.

4- Serum calcium and iron: Serum calcium level was measured by using serum calcium kit (Syrbio)

with the mean levels of iron in breast cancer patients. These differences may be result from genetic effect Elevated serum iron might indicate the presence of malignant disease and could be regarded as a predictor of positive lymph node involvement in patients with breast cancer. (16). Table (3) showed significantly ($p<0.05$) increased level of serum ALP in both patients compared with the normal subjects.

DISCUSSIONS:-

Table (1) showed mean values of serum calcium in both breast cancer and leukemia in relation to the age. There is significant differences ($p<0.05$) between the three groups of patients compare with the groups of normal individuals. But there were low mean values of serum within the three groups of the breast cancer comparing with the mean values in leukemia patients this is an agreed with the conclusion of Keshaviah et al and Cavenee (12, 13). Malignancy-associated hypercalcemia may be divided into three major categories: humoral hypercalcemia mediated by parathyroid hormone-related protein (PTHrP), hypercalcemia induced by dysregulated production of calcitriol, and local osteolytic hypercalcemia in which there is activation of osteoclasts in the vicinity of tumor cells in bones (14). The study of the etiologies of high serum ALP can be useful data in diagnosis. The elevation of serum ALP occurs because of the accelerated de novo synthesis of the enzyme and subsequent regurgitation into the serum.(1,2). In breast cancer increased serum ALP may be due to many factors several growth factors and hormones were shown to modulate the expression and activity of ALP in various tissues and cultured cells (18). in breast cancer the mean levels of enzyme was higher than in leukemia within the three groups of age may be result from increased concentration of iron binding proteins in these patients. (17). and also many other Hormone factors effect ALP levels and hormone effect should be much more rapid, Tsu-Chung CHANG et al (18). Suggest that mediator proteins are involved in the regulation of ALP expression in BC-MI cells. Regulation of ALP gene expression by hormones and various agents occurred in different cells or tissues by a variety of mechanisms. Increased levels of ALP depend on the severity of diseases, and the enzyme and subsequent regurgitation into the serum.

Table (1) Serum calcium levels in patients and normal subjects in relation to the age

Age (year)	Leukemia Mean ± SD Mg/dl	Breast cancer Mean ± SD Mg/dl	Normal subjects Mean ± SD Mg/dl
25-50 (group 1)	17.00 ± 3.75**	13.71 ± 3.51*	7.00 ± 0.5
50-55 (group 2)	13.80 ± 1.99*	10.76 ± 1.72*	8.30 ± 0.53
55-70 (group 3)	18.54 ± 5.00**	15.00 ± 1.90**	7.31 ± 0.37

* Significant values, ** highly significant values

Table (2) Serum iron levels in patients and normal subjects in relation to the age

Age (year)	Leukemia Mean ± SD µg/dl	Breast cancer Mean ± SD µg/dl	Normal subjects Mean ± SD µg/dl
25-50 (group 1)	185.51 ± 45.20**	178.81 ± 48.22**	100.20 ± 24.00
50-55 (group 2)	170.11 ± 35.41**	195.15 ± 46.11**	98.35 ± 21.11
55-70 (group 3)	191.81 ± 43.38**	182.41 ± 44.31**	168 .00 ± 34.50

* Significant values, ** highly significant values

Table (3) Serum Alkaline phosphatase levels in patients and normal subjects in relation to the age

Age (year)	Leukemia Mean ± SD U/L	Breast cancer Mean ± SD U/L	Normal subjects Mean ± SD U/L
25-50 (group 1)	70.62 ± 3.40*	155.01 ± 21.00 **	40.00 ± 13.22
50-55 (group 2)	96.00 ± 11.55*	198.54 ± 27.25 **	60.82 ± 9.65
55-70 (group 3)	82.79 ± 10.7 *	185.33 ± 31.21**	33.17 ± 5.99

* Significant values, ** highly significant values

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