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Detection of Ovarian Cancer by Osteopontin and CA-125 in Al- Najaf and Karballa Provinces/Iraq

Zainab Sajid Mohammed[(1)] , Hasanain Jalil Kadhim[(2)], Radhwan M. Hussein[(1)] , and Abdul Hadi Salal [(3)] .
[1]Ahlulbait university/Iraq / College of Pharmacy-Karballa , [2]College of Tussi University/Iraq , [3] Islamic University , Najaf/Iraq

Abstract

Ovarian cancer is the fifth leading cause of death from cancer among North American women, and Ovarian cancer is one of the most common reproductive cancers and has the highest mortality rate amongst gynecologic cancers.

Aim: To discover new biomarkers of ovarian cancer in order to surmount the obstacles in early-stage diagnosis.

Method: The present study was elevated in Middel Euphrates cancer center and Al-Sader medical city in al Najaf province and Imam Hussein Teaching Hospital Al-Hussein center for the treatment of tumors and blood diseases respectively , since between march 2016 and June 2017, total ovarian cancer woman where included in this study. The study involved one hindered and sixty (160) women, who were distributed into two groups of patients (benign and malignant) that diagnosed to 60 cases benign tumor and 100 cases malignant tumor and disrupted according to age groups between 15 and 65 years .The diagnosis was made by the consultant medical staff , and third group of women was enrolled in the study as control (healthy woman) .The results revealed comparison results between Al-Najaf and Al-Karballa provinces according to type of tumor in Najaf 45 (45.0%) malignant and 25(42.0%) benign ,while for Karballa 55 (55.0%) malignant and 35 (58.0%) benign. Also levels of tumor marker osteopontin when compared with control group (healthy woman)

Results: high significance ($p<0.05$) in Malignant ovarian cancer about (65.1317±1.4972) that mean while in benign tumor was that mean (63.6728 ± 1.3180) with tumor marker osteopontin**.** Significant increase ($p<0.05$) in levels of ALT , AST , ans ALP in benign and malignant cancer group when compared with control group.

Keywords : Cancer antigen -125, Liver function tests, Ovarian cancer, Osteopontin.

INTRODUCTION:

Furthermost patients with ovarian cancer will be die from their disease, it is neither a communal nor a rare disease, At any rate in part cause 75% to 80% of all patients present with late-stage disease, for which current treatment is inadequate (1). In 2004 some 25.580 woman will be diagnosed with ovarian cancer in USA and 16.90 will die from the disease, the national comprehensive care network guidelines for post-treatment surveillance of woman with ovarian cancer are the current standard of care in the United States (2) These guidelines recommend office visits every 2-4 months for the first two years and then 3-6 months for the following three years. Each visit includes a full interval history and a physical exam aimed at detecting recurrence (3).

Osteopontin (OPN) is expressed in a variety of normal and tumor tissues, (4) including ovary, bone (5) breast,(6) prostate,(7), uterine endometrium,(8) lung,(9) kidney,(10) and and has been assessed as a potential diagnostic marker in malignancy.(11) A large number of hormones and cytokines – such as estrogen, progesterone,(8). Osteopontin is known to be involved in a variety of physiological cellular functions such as tumorigenesis, metastasis, and angiogenesis (5).

Screening markers, such as CA-125, is limited by the fact that no single marker is up-regulated and shed in adequate amounts by all ovarian cancers. Although CA-125 represents the best available serum marker, achieving 50% sensitivity and 99% specificity for early –stage disease, it detects only 80 % of all ovarian cancer (12). In reality , epithelial ovarian cancer is a heterogenous disease. Histological subtypes of the epithelial cancer as well as serous, endomaterioid, mucinous and clear cell carcinomas are known to have different clinical characteristics as well as different molecular features as well as different molecular features (12). Then, a panel of complementary tumor markers will be required to detect all cases of ovarian cancer at an early stage. If screening is to be performed with individual assays, a limited number of markers must encompass the heterogeneity of the disease (13).

Cancer antigen -125 levels and transvaginal ultrasonography (TV-USG) can underwrite to the early detection of ovarian cancer. Unfortunately, these tests are not currently cost-effective; they are thus not used routinely to screen ovarian cancer (14).

For ovarian cancer , endometrial , and cervical cancers , it is critical to detect the disease at the earliest possible stage. The discovery of useful serum biomarkers for the early detection of gynecologic cancers has thus been a high priority . such tumor markers will be molecules arising from the presence of a tumor , which can appear in the surrounding tissue, and then within the blood and excretions (10).

MATERIALS AND METHODS:

Blood sample

Venous blood sample were collected into gel tubes without anticoagulant , serum was separated by centrifuge immediately after clotting and stored in -30 degree centigrade until assayed.

Tumor markers (CA-125 & OPN)

The concentration of tumor markers CA-125 and OPN were estimated by Mini VIDAS CA-125 and OPN ELISA kits (BioMerieux , France).

Liver function test:

Determined the coloric of aspartate transaminase and alanine transaminase activity according to the Reitman and Frankel way , by using Syrbio diagnostic reagents kit (Reitman and Frankel, 1957). According to kind and king (1954) method we determined the colorimetric of ALP by using Biomerieux kit.

Bio-statistical analysis

The outcomes were stated as "mean ± standard deviation ,t- test "was used for the contrast between control and other assemblies in the stately parameters, one way examination of variance (ANOVA) followed by least significant difference (L.S.D.) analyses at 0.05% probability of levels.

RESULTS:

One hindered and sixty (160) were outpatients department and Al-Furrat Al-Awsat hospital of tumor center in Al-Najaf city , and imam Hussein hospital in Karballa province . This 160 women patients diagnosed to 60 cases benign tumor and 100 cases malignant tumor and disrupted according to age groups. High frequency in age group in >55 for benign (35.0%), and malignant (36.0%),while, low frequency in age group <35 for benign (12.0%), and malignant (12.0%).show table (1).

The results in table (2) revealed significant differences at ($p<0.05$) between Al-Najaf and Al-Karballa provinces according to type of tumor for in Najaf 45 (45.0%) malignant and 25 (42.0%) benign ,while for Karballa 55 (55.0%) malignant and 35 (58.0%) benign.

Table (1) : Distribution type of tumor according to age groups:

Type of tumor	Age	Frequency	Percent %
Benign	<35	7	12.0
	36-45	15	25.0
	46-55	17	28.0
	>55	21	35.0
	Total	**60**	**100.0**
Malignant	<35	12	12.0
	36-45	22	22.0
	46-55	30	30.0
	>55	36	36.0
	Total	**100.0**	**100.0**

Table (2) : Comparison between Al-Najaf and Karballa according to type of tumor .

Type of tumor	Province	Frequency	Percent %
Benign	Najaf	25	42.0
	Karballa	35	58.0
	Total	60	100.0
Malignant	Najaf	45	45.0
	Karballa	55	55.0
	Total	100	100.0

The results in this figure (4-1) demonstrate there are high significance (p<0.05) in Malignant ovarian cancer that mean (78.6300±1.8577) while in benign tumor was that mean (71.9978±0.3548) with tumor marker osteipontin acorrding to their age .

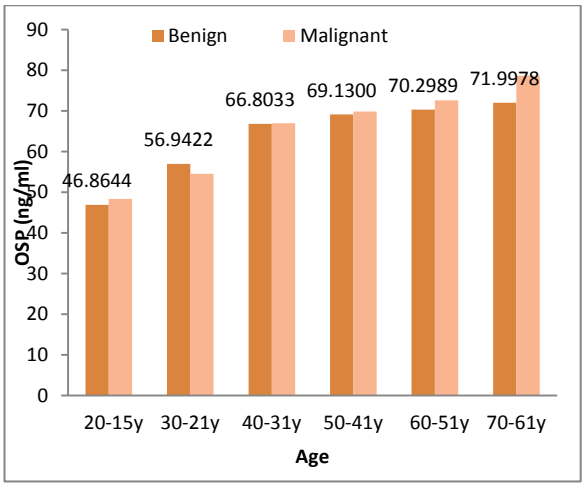

Figure (1): Levels of OSP in woman pateints accorrding to age in benign and malignant tumor

The results in figure (2) revealed comparison between benign and malignant tumor in woman pateints according to levels of tumor marker osteopontin when compared with control group (healthy woman), there are high significance (p<0.05) in Malignant ovarian cancer about (65.1317±1.4972) that mean while in benign tumor was that mean (63.6728 ± 1.3180) with tumor marker osteopontin**.**

The results in figure (3) revealed comparison between benign and malignant tumor in woman pateints according to levels of tumor marker CA-125 when compared with control group (healthy woman), there are high significance (p<0.05) in Malignant ovarian cancer about (462.00±12.01) that mean while in benign tumor was that mean (208.40 ± 33.42) with tumor marker osteopontin.

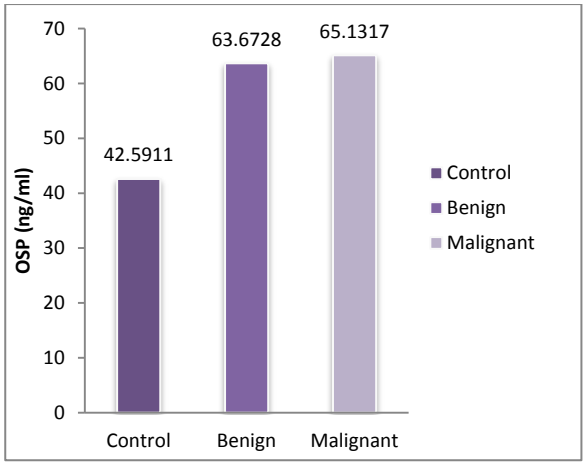

Figure (2): comparison between benign and malignant tumor according to OSP levels.

Also the results that revealed in figure (4) for descript comparison between the cases was with benign 60 which mean (126.850± 8.732), whereas malignant 100 was mean (280.135 ±15.370) in malignant with CA-125 levels, this results statistically revealed high significance (p <0.05) when compared with control (28.714±1.683).

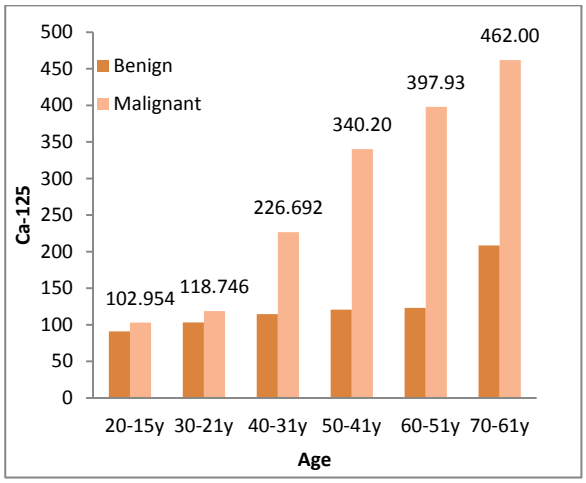

Figure (3): Levels of CA-125 in woman pateints accorrding to age in benign and malignant tumor.

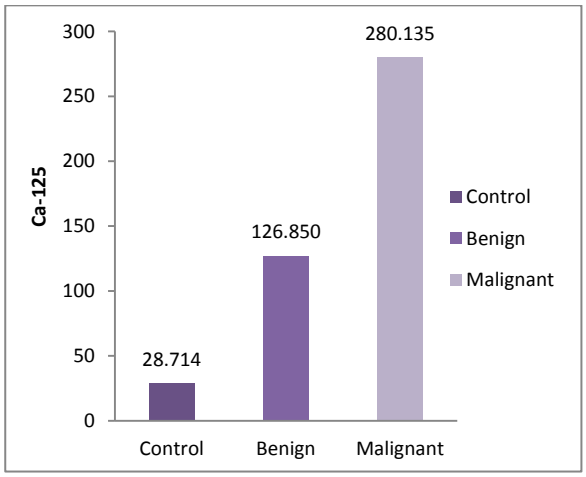

Figure (4) Comparison between benign and malignant tumor in woman pateints according to levels of tumor marker CA-125

Liver function tests:

The results in figure (5) releaved significant increase ($p<0.05$) in levels of ALT (72.027 ±2.63) in benign cancer group when compared with control group, but high significant increase in malignant cancer group (112.25 ±3.47) when compared with benign and control groups.

Also the results in the figure (6) revealed AST levels of the cases was with benign 60 which mean (49.423± 1.374), whereas malignant 100 was mean (84.723±2.217) in malignant with urea levels, this results statistically revealed high significance ($p<0.05$) when compared with control (31.83±2.47).

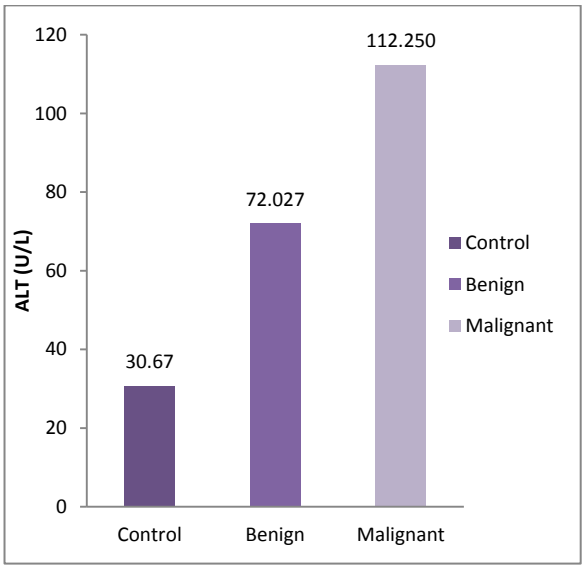

Figure (5):Levels of ALT in woman pateints in benign and malignant tumor

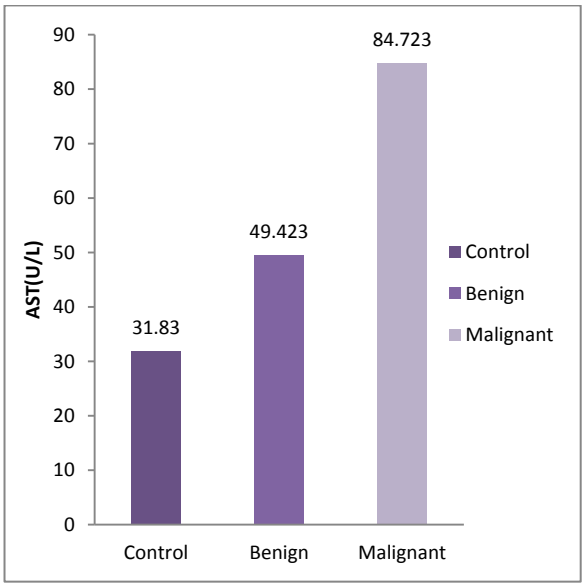

Figure (6):Levels of AST in woman pateints in benign and malignant tumor.

As it is shown in the figure (7) ALP levels of the cases was with benign 60 which mean (105.348± 1.188), whereas malignant 100 was mean (128.170 ±2.764) in malignant with urea levels, this results statistically revealed high significance ($p<0.05$) when compared with control (68.43±7.69).

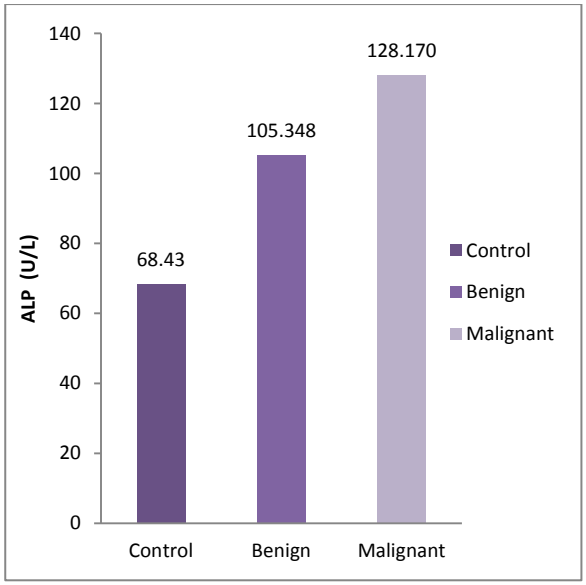

Figure (7):Levels of ALP in woman pateints in benign and malignant tumor.

DISCUSSION

Ovarian cancer is a major cause of morbidity and mortality among the gynecological malignancies ovarian carcinoma is difficult to diagnose and it is usually discovered only in its advanced stages. It therefore has the highest mortality among all gynecological malignancies. (15). Osteopontin (OPN) is known to be involved in a variety of physiological cellular functions such as tumorigenesis, metastasis, and angiogenesis (5).

In the results of this study we evaluated the high levels of OPN When compared with levels of CA-125 in woman patients showed more significant and high specifically for detection ovarian cancer due to concordance between Osteopontin expression rank and stage or grade rank was 67–84% over all types of cancer. This is comparable to the accuracy commonly estimated for existing tumor markers, including CEA, CA 15-3, CA 19-9 and PSA, this indicated OPN more specific for detection ovarian cancer than other markers (16).

Also present high levels of CA-125Though an elevated CA125 level should raise a suspicion of ovarian cancer, its interpretation in patients with any serosal involvement may not be easy, since any type of pleural, peritoneal or pericardial irritation can lead to elevated serum level of this high molecular weight glycoprotein (17). As mentioned above, an elevated CA125 level is not a specific diagnostic marker for ovarian cancer as it may be elevated in a cirrhotic patient, due to peritoneal irritation. Thus, extremely high CA125 levels merit further investigation. The pharmacokinetic disposition of chemotherapy in patients with ovarian cancer, drugs is known to be metabolized by the liver and subsequantly excreted in the bile, primarily as metabolites. Some of the metabolites are pharmacologically active and possess 10% to 25% of the hypotensive .Therapy with chemotherapy should be administered cautiously in patients with significantly diminished hepatic or biliary function, since drug and/or metabolite accumulation may occur, continuous therapy may be administered cautiously in patients with impaired hepatic function or progressive liver disease this due to increased levels of liver enzymes.

Also attributed to various factors including metabolic changes associated with stress, loss of appetite and under certain condition, immune reaction developed against the individual's own tissues, leaking to autoimmune disease auto-antigens evoke a self-perpetuating immune reaction that results in chronic tissue

damage and inflammation, non-immune mediated inflammation due to interaction or tissue with trauma.

CONCLUSIONS

Early detection of ovarian cancer could have a major impact on the disease. Demonstrate The results for malignant ovarian cancer in Al-Karball province is more highly than Al-Najaf province , also revealed OPN and CA-125 levels were associated with ovarian neoplasm , and their significant increase in patients could be helpful in early detection of O.C.

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