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Evaluate the Levels of Fas-associated Factor 1 and the Oxidation State of Breast Cancer Women

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Abstract

The current study aims to evaluate the levels of Human FAS-Associated Factor, Uric Acid, Glutathione Peroxidase and Malondialdehyde in sera of women with breast cancer-BC; ninety serum samples were collected from women. They were divided into three groups, the control group-C includes 30 samples of healthy women with no history of breast cancer, 30 samples of women newly diagnosed with breast cancer (as first group-G1), and 30 samples of women with breast cancer who underwent chemotherapy (as second group-G2). The study includes the determination of the level of serum FAS-Associated Factor, Uric Acid, Glutathione Peroxidase and Malondialdehyde. The results indicate that the value of body mass index-BMI and UA level were significantly ($P \leq 0.05$) increased in G1 as compared with G2 and C. The levels of FAF1 and MDA were significantly ($P \leq 0.05$) elevated in the patients' group as compared with C, with no significant ($P \leq 0.05$) difference for serum GPX activity between patients and the control group. We can conclude from the results of the current study that the FAF1 and MDA were associated with an increased risk of breast cancer. Also, UA plays an important role in the development of breast cancer.

Introduction:

The incidence of breast cancer-BC is gradually increasing worldwide at a rate of 1% per year. Still, the death rate is decreasing due to the introduction of effective and new treatment regimens that prolong survival and also improve quality of life. BC affects 30% of women over the age of 70 [1]. Breast cancer includes several types, and sometimes a tumor is a combination of more than one type. It is diagnosed in several ways in its early stages, such as magnetic resonance imaging-MRI, ultrasound, biopsy, mammography-MMG and Clinical cancer examination-CCE [2]. Signs of BC can include a change in the shape of the breast, a lump in the breast, fluid secretion from the nipple, and swelling of the lymph nodes under the

armpit [3], and can be classified into two groups: invasive and non-invasive, and it is located either in the lobes (within the lobes) or ducts [4]

Fas-associated factor-1 (FAF1) is a proapoptotic protein that binds to Fas and is involved in the formation of the death-inducing signaling complex during apoptosis mediated by FAS. It plays a critical role in normal development and also in the survival of the neuronal cell; the downregulation of FAF1 may participate in many sides of tumor genesis, which contributes to preventing cancer development [5]. Increasing the level of FAF1, may increase the apoptosis of the cells and then induce the oxidative stress of the cells [6,7]. Evaluate the correlation between high FAF1 and antioxidants state in patients with BC is a main aim of the study.

Subjects and methods:

The study includes the determination of the concentration of serum FAF1 (using enzyme-linked immunosorbent assay-ELISA), Uric Acid-UA, Glutathione Peroxidase-GPX and Malondialdehyde-MDA (by using spectrophotometric colourimetric methods) [8-11].

Data obtained were analyzed using Duncan's multiple range tests via the statistical package of the social sciences program-SPSS, and a P ≤0.05 was considered statistically significant.

Results and Discussion:

The results of the present study were summarized in table 1.

Table 1: Mean±SD of FAF1, UA, GPX and MDA levels in sera of groups under investigation

Parameters	Control group-C	First group-G1	Second group-G2
Age (year)	45.666±7.023a	48.966±11.189a	47.900±9.721a
BMI(Kg/m^2)	30.841±5.050b	32.093±6.934a	29.019±4.91b
FAF1(ng/ml)	11.970±3.172c	17.446±5.221b	22.462±3.692a
UA(mg/dL)	4.776±1.192b	5.886±1.417a	4.613±1.438b
GPX(U/L)	2.080±1.388a	2.156±1.592a	2.107±1.659a
MDA(µmol /L)	7.189±3.583b	16.126±8.784a	13.041±7.456a

Level of serum FAF1

The level of Fas-associated factor-1-FAF1 significantly (P ≤0.05) increased in (G1 and G2), with a significant rise after chemotherapy session(G2) compared with G1, Figure 1.

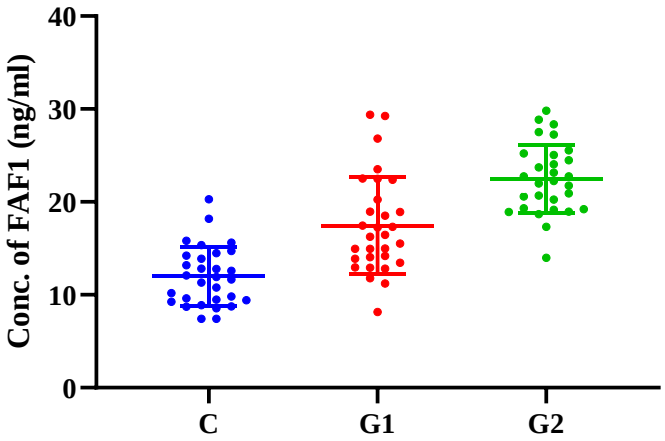

Fig. 1 Serum level of Fas-associated factor-1.

The conserved protein FAF1 plays a critical function in the *progression* of normal and survival of the neuronal cell and also may contribute to the many aspects of tumor genesis by down regulation of FAF1[5]. Some studies indicate that the loss of FAF1 is a prevalent occurrence in some types of human cancer, and FAF1 is implicated as a tumor suppressor that contributes to apoptosis regulation, so it is down regulation would be expected to induce the tumor survival of the cell and also induce the resistance for the anticancer drugs effect [12].

The finding of the current study about the level of FAF1 was agreed with the finding of [13]. in which the overexpression of Fas-associated factor-1 can decrease the invasion and metastasis of tumors in the breast tissue. That way, the down-regulation of Fas-associated factor-1 has a close relationship with raised metastasis in BC. No information about the level of serum FAF1 in sera of women with breast cancer was available in the literature, so more studies were needed to clarify the correlation between FAF1 and BC.

Level of uric acid

The significant (P ≤0.05) elevation was shown in the present study's results in the serum uric acid level in G1 compared with G2 and C, Figure 2.

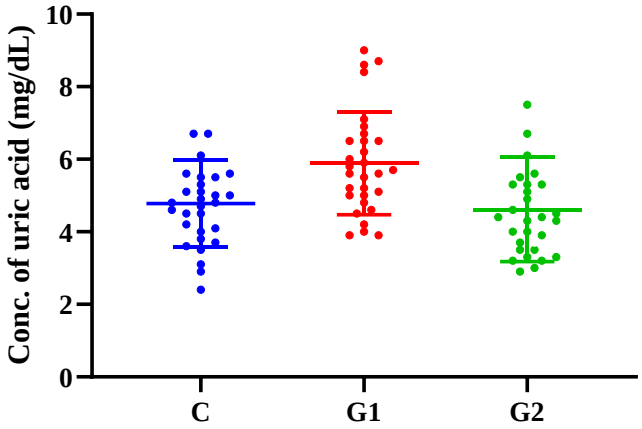

Fig. 2 Serum level of uric acid.

The final metabolic product of purine metabolism is UC. Many researchers evaluate the role of UA in breast cancer [14, 15]. The study`s findings agreed with the results of Yue *et al*.[16], suggesting that the elevation in serum concentration of uric acid predicts a poor survival rate among women with BC. Some studies indicate that high levels of UA are associated with excess risk of cancer, mortality and recurrence of the disease [16,17]. Whilst it is known that uric acid acts as a systemic antioxidant, the pro-inflammatory properties of UA have been presumed to play a critical role in cancer pathogenesis [17].

The decreasing serum UA levels in sera of women with BC undergoing chemotherapy may be due to the diet. Insufficient intake during treatment, which acts as an exogenous antioxidant source [18], leads to consuming the uric acid that scavenges the free radicals(superoxide, peroxyl and hydroxyl radicals) and prevents the oxidation of biochemical molecules that include lipids, proteins and nucleic acid[19].

Activity of glutathione peroxidase:

Table 1 showed that the activity of serum glutathione peroxidase-GPX didn't show any significant difference among the three groups (patients and control group), As in Figure 3.

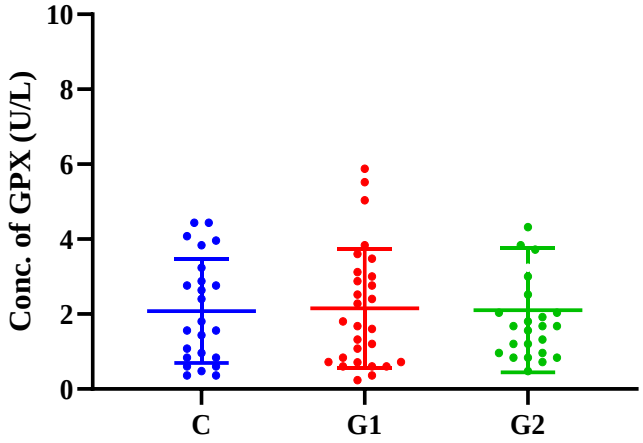

Fig. 3 Activity of glutathione peroxidase.

Glutathione peroxidase is an antioxidant defense system that prevents, reduces or retard the oxidation of biochemical molecules in living cells that may be exposed to the risk of oxidation. Antioxidants are chemical compounds that prevent or retard the damage of reactive oxygen species-ROS on target tissues, Its divided into two categories:

-Endogenous antioxidants (Non-enzymatic type) such as uric acid, albumin, glutathione, etc.

-Endogenous antioxidants (Enzymatic type) such as superoxide dismutase-SOD, glutathione peroxidase and catalase-CAT [20].

The finding of the study indicates that the GPX activity not be affected by the disease, this finding was disagreed with the finding of [21,22], which suggest that the increase in GPX activity may be due to the increase the gene expression for GPX.

Level of malondialdehyde

The concentration of MDA significant (P ≤0.05) elevated in the (G1 and G2) compared to healthy individuals in C, Figure 4.

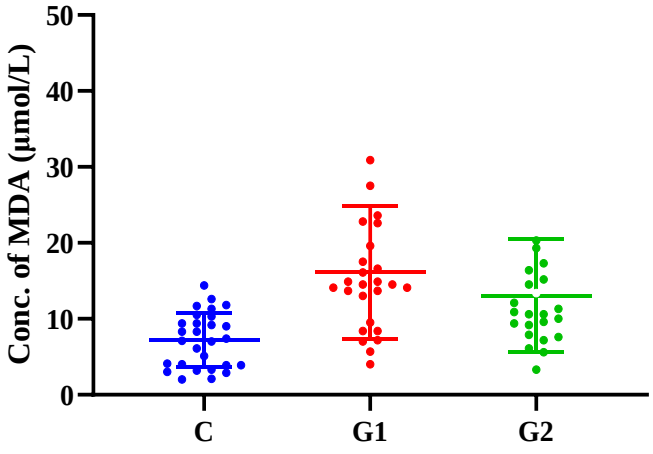

Fig. 4 Serum Level of Malondialdehyde.

These obtaining results agreed with the results of many studies [23-25], which indicate an increase in the concentration of serum MDA in patients with BC. MDA is an essential marker for lipid peroxidation and increases the oxidative stress in living cells, in which the high free radicals increase the risk of cancer [24].

Conclusions

The conclusion from all the study results was that FAF1 and MDA were associated with an increased risk of BC. Also, uric acid plays an essential role in developing breast cancer groups (G1 and G2) compared with C, while the correlation between GPX and breast cancer is obscure.

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تقييم مستويات العامل المرتبط FAS-1 وحالة الأكسدة لدى النساء المصابات بسرطان الثدي

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الخلاصة:
تهدف الدراسة الحالية إلى تقييم مستويات العامل المرتبط بـ FAS-1 البشري FAF1 وحمض اليوريك-UC والجلوتاثيون بيروكسيديز-GPX والمالونديالدهيد-MDA في أمصال النساء المصابات بسرطان الثدي-BC، وجمعت تسعون عينة مصل من النساء. وقسمت إلى 3 مجموعات، المجموعة الضابطة-C تضم 30 عينة من النساء الأصحاء وليس لديهن تاريخ للإصابة بسرطان الثدي، و30 عينة من النساء اللاتي شخصت إصابتهن بسرطان الثدي حديثًا (كالمجموعة الأولى-G1)، و30 عينة من النساء المصابات بسرطان الثدي اللاتي خضع للعلاج الكيميائي (المجموعة الثانية-G2). تتضمن الدراسة تحديد مستوى المصل FAF1، UA، GPX وMDA. تشير النتائج إلى أن قيمة مؤشر كتلة الجسم ومستوى UA قد زادت بشكل ملحوظ (P ≥0.05) في G1 مقارنة مع G2 وC. بينما كانت مستويات FAF1 وMDA مرتفعة بشكل ملحوظ (P ≥0.05) في المرضى. المجموعة بالمقارنة مع المجموعة C، مع عدم وجود فرق معنوي (P ≥0.05) في نشاط GPX في المصل بين المرضى والمجموعة الضابطة. يمكننا أن نستنتج من نتائج الدراسة الحالية أن FAF1 وMDA ارتبطا بزيادة خطر الإصابة بسرطان الثدي. ويلعب UA دورًا مهمًا في تطور سرطان الثدي..