Original Article

Serum Protein Levels and Albumin/Globulin Ratio in Patients with Uterus, Ovary, and Breast Tumors Compared to Healthy Women in Kirkuk City

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Abstract

Background: Gynecological cancer is one of the most serious public health problems in the world with main gynecological cancers, uterus, breast, and ovarian, causing morbidity with severe suffering and a high mortality. **Objective:** This study aimed to investigate the levels of the total protein (TP), albumin (Alb), globulin (Glo), and Alb/Glo ratio in the female patients with (uterus, ovary, and breast) cancer compared to healthy females. **Materials and Methods:** This study included 120 females with (28 uteri, 31 ovaries, and 25 breasts) cancer patients and 36 healthy control participants, with age ranges between (20 and 42) years. **Results:** Alb levels significantly ($P \leq 0.05$) decreased in all patient samples except those with uterus cancer who showed significant increase ($P \leq 0.05$) compared to healthy participants, and Glo levels significantly ($P \leq 0.05$) decreased for uterus and breast cancer samples and nonsignificant ($P \leq 0.05$) decrease in patients with ovary cancer compared to healthy participants; finally, the ratio of Alb./Glo. showed significant ($P \leq 0.05$) decrease in all patients group except patients with breast cancer showed significant increase ($P \leq 0.05$) compared to healthy participants. The results of correlation coefficient indicated that there were significant ($P \leq 0.05$) positive correlations between TP and Glo for uterus and breast cancer patients and between TP and Alb for ovary cancer patients. **Conclusion:** The ratio of Alb/Glo was significantly ($P \leq 0.05$) decreased in all patients group except patients with breast cancer who showed significant increase ($P \leq 0.05$) compared to healthy participants which could be used in the diagnosis of these patients.

Keywords: Albumin/globulin ratio, breast cancer, ovary cancer, uterus cancer

Introduction

Two major types of proteins present in the serum are "albumin (Alb) and the globulin (Glo)." Alb is the major type of serum protein component.[1] The role of Alb is, however, controversial as yet and Alb use may be based more on custom than on a scientific basis, due to its limited availability and high cost, it is important that the use of Alb is limited to hint for which it is efficacious.[2] Alb was synthesized in abundant amount in the liver, form about 60% of all serum proteins,[3] its water-soluble protein with important functions in regulating the volume of blood by preserving the oncotic pressure (colloid osmotic pressure) of the blood compartment,[4] and also Alb has a function as carrier for many hydrophobic molecules, such as bile salts, steroid hormones, free fatty acids as (apoprotein), unconjugated bilirubin, metals (Ca, Zn, and Cu), and some drugs including phenylbutazone, warfarin, and phenytoin.[5] Serum Glo divided into: alpha (α) and beta (β) Glos are synthesized exclusively in the liver and gamma (γ) Glo is synthesized by B-lymphocytes; all types of Glos are broken down by lthe iver.[6] Gamma Glo presents as a largest proportion from other Glo types.[7] Many confusing factors may effect on the levels of "Alb and Glo" which may influence the accuracy and efficiency in detection of them. A novel prognostic index, the Alb/Glo ratio (AGR), was specified and notified.[8,9] AGR is a component of them and suggested to be more steady and authoritative than serum Alb or Glo alone.[10,11] Numerous researchers were promising AGR as tumor marker in diverse types of cancers.[7,10-13] Breast cancer is quite heterogeneous malignant disease with combination

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"etiological and pathological characteristics." It is the most common cancer in women and a major public problem of health.[14] Ovarian cancer is the most fatal gynecological cancer and more heterogeneous than breast cancer.[15] Uterine cancer also known as "endometrial cancer" is the most occurring sexual tract malignancy of female in the world.[16] However, according to our knowledge, no study has been conducted to clarify the clinical significance and prognostic value of this marker AGR in "ovarian, uterine, and breast" cancer in Kirkuk city; for this reason, this study was carried out to evaluate and assess the concentration of total protein (TP), Alb, and Glo among women with breast and gynecological cancers (ovary and uterus) compared to healthy participants.

Materials and Methods

Study area and time

This study was carried out in the Azadi Teaching Hospital, Kirkuk, Iraq, from the period, December 2016 to September 2017.

Collection of blood

A total of 84 women comprising 28, 31, and 25 patients with breast, ovary, and uterus cancer, respectively, age ranges between (20 and 42) years; after being classified by senior surgery and histologically diagnosed (patient suffering from any disease that may interfere with this study were excluded), 36 healthy women with the same age ranges as patients were selected and enrolled into this study. Five milliliters of venous blood was collected from each participant aseptically into a plain container. Samples were allowed to clot, spun at 1500 × g for 10 min, and serum obtained and kept frozen until required for analysis. Ethical approval was given by the Institution Ethical Committee of Azadi Teaching Hospital. Blood samples were collected for testing of TP, Alb, and Glo before starting treatment for patient samples.

Biochemical analysis

Total serum proteins, Alb and Glo, were determined spectrophotometrically using Biuret and bromocresol green methods by Doumas *et al*.[17] Alb/Glo ratio was also determined by dividing Alb on Glo. All reagents were products of Randox Laboratories UK.

Statistical analysis

Descriptive statistics were used in analyzing the patient's characteristics and laboratory parameters for each group. In addition, unpaired Student *t*-test was used to assess group differences, where appropriate. A statistical significant difference was accepted as $P < 0.05$. All the statistical analyses in this study were made using GraphPad Prism 6.0 program (GraphPad Software, San Diego, CA, USA).

Results

Table 1 showed the (mean ± standard deviation) serum "TP, Alb, Glo, and Alb/Glo ratio" to all studied groups.

From Table 1, the results indicated that the levels of TP were significantly ($P \leq 0.05$) decreased for all patient samples compared to healthy participants; Alb levels were significantly ($P \leq 0.05$) decreased in all patient samples except those with uterus cancer showed significant increase ($P \leq 0.05$) compared to healthy participants; Glo levels were significantly ($P \leq 0.05$) decreased for breast cancer samples and nonsignificantly ($P \leq 0.05$) decrease for uterus cancer, while patients with ovary cancer showed significant increase ($P \leq 0.05$) compared to healthy participants; finally, the ratio of Alb/Glo showed significant ($P \leq 0.05$) decrease in all patients' group except patients with breast cancer showed significant increase ($P \leq 0.05$) compared to healthy participants. Table 2 and Figure 1 represent the correlation coefficients and *P* values for all patient groups and to all parameters.

The results indicated that there were high positive significant $P \leq 0.05$ correlations between TP and Glob for (uterus, breast, and ovary) cancer patients and between TP and Alb. In addition, a negative significant correlation was observed between Alb and Glob in breast patients.

Discussion

This study compared the TP, Alb, and Glob levels, and the Alb/Glo ratio in patients with (uterus, ovary, and breast) cancers compared to healthy women in Kirkuk city. In the present study, there was significant decrease in TP level for all patient groups compared to healthy participants. Al-Muhtaseb[18] and Ibrahim *et al*.[19] found that there was an increase in the TP level in the serum of female patients with breast cancer. Watanabe *et al*.[20] demonstrated that the circulating rapid turnover protein levels were decreased in advanced stages of ovarian cancer. Al Byati *et al*.[21] indicated that there was nonsignificant difference ($P > 0.05$) in TP levels in all patients groups (uterus, ovary, and breast cancer) as compared to healthy participants. Alb and Glo "major components of serum proteins" could be used as a useful

Table 1: "Total protein, albumin, and globulin" levels and albumin/globulin ratio in the sera of all studied groups

Groups	*n*	TP (g/dl), mean±SD	*P*	Alb (g/dl), mean±SD	*P*	Glo (g/dl), mean±SD	*P*	Alb/Glo, mean±SD	*P*
Uterus cancer	28	67.93±7.292	0.004*	44.08±0.26	0.0017*	30.80±3.22	0.056**	0.032±0.1	0.02*
Ovary cancer	31	69.9±0.9	0.0002*	30.73±9.45	0.0002*	37.08±0.56	0.0257*	0.828±0.034	0.034*
Breast cancer	25	68.88±0.87	0.0115*	42.0±4.8	0.0480*	29.79±21.3	0.0228*	1.41±5.7	0.05*
Healthy participants	36	72.67±4.323		43.16±0.768		32.01±0.484		1.35±3.74	

*$P \leq 0.05$ (significant), **$P \geq 0.05$ (nonsignificant). TP: Total protein, SD: Standard deviation, Alb: Albumin, Glo: Globulin

Table 2: Correlation coefficient and *P* value for all patients groups

Groups	*R*	*P*
Uterus cancer		
TP-Alb	0.5161	0.005*
TP-Glo	0.6414	0.0002*
Alb-Glo	−0.2830	0.14**
Ovary cancer		
TP-Alb	0.6955	0.002*
TP-Glo	0.5415	0.001*
Alb-Glo	−0.2274	0.22**
Breast cancer		
TP-Alb	0.3016	0.14**
TP-Glo	0.7134	0.001*
Alb-Glo	−0.4531	0.023*

*$P \leq 0.05$ (significant), **$P \geq 0.05$ (nonsignificant). TP: Total protein, Alb: Albumin, Glo: Globulin

prognostic marker and as a predictor of tumor progression and survival, respectively, in cancers, such as "ovarian cancer, gastric cancer, lung cancer, and colorectal cancer."[22]

The results of this study for Alb and Glo were revealed that there was significant decrease in Alb for ovary and breast cancer patients whereas there was significant increase in uterus cancer patients; the above results were disagreed with Al Byati *et al*.;[21] they mentioned that there was significant decrease in Alb levels in patients with uterus cancer and nonsignificant difference in breast and ovary cancer patients as compared to normal participants and also found a nonsignificant difference in Glo level in all patients groups and as compared to normal participants. Several studies found that low serum Alb was a negative foreteller of whole survival rate in several tumors[23] such as colorectal,[24-26] gastric,[27] pancreatic,[28,29] hepatocellular, breast,[23,30] lung,[23] and ovarian.[23,31] The

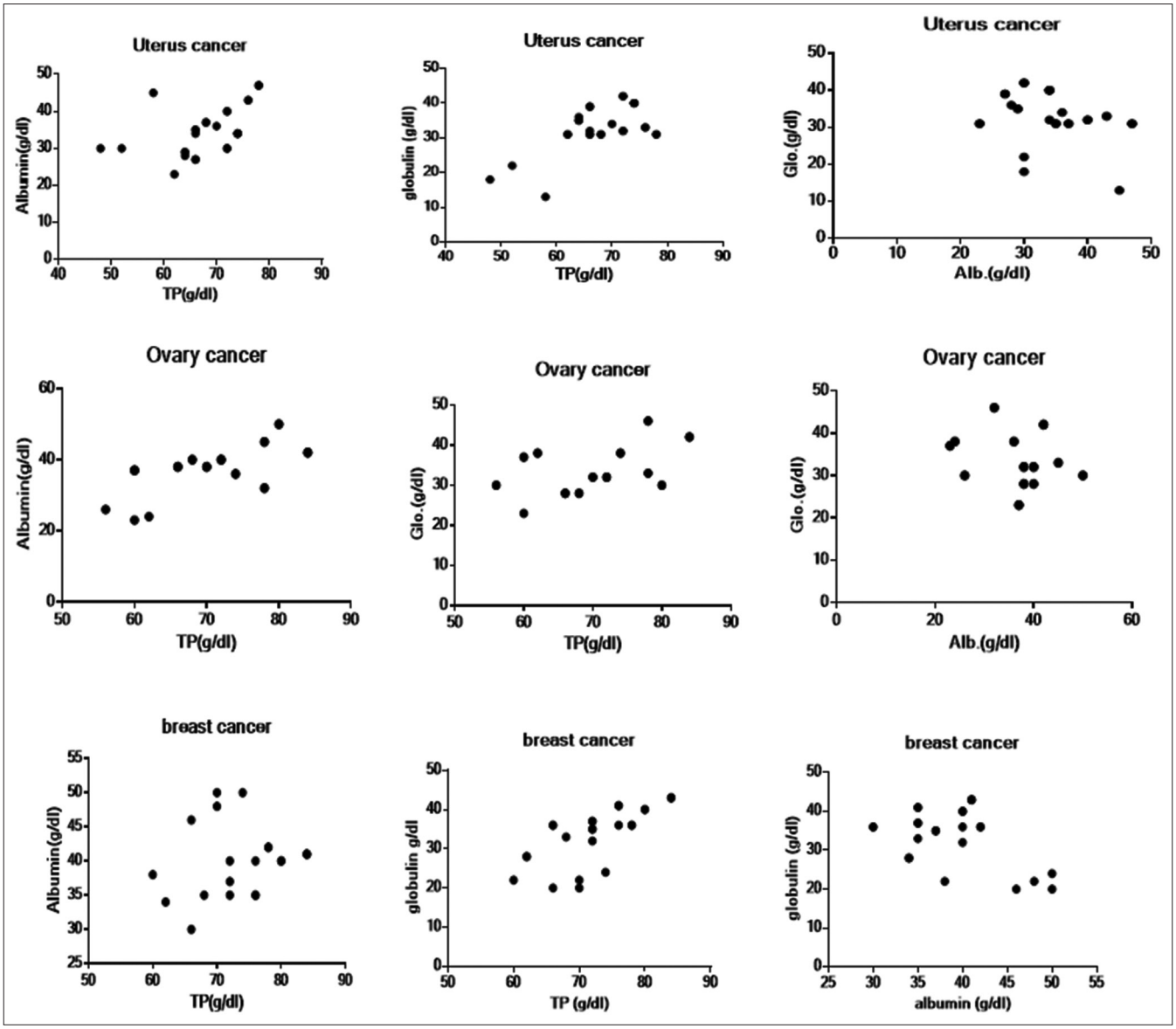

Figure 1: Correlation coefficient between serum total protein with (albumin and globulin) and between albumin and globulin

decrease in serum Alb level may lead to hypoproteinemia or malnutrition; also, the "survival duration and life quality" of patients with cancer may effect.[32]

The evaluation of both "Alb and Glo" levels in cancer patients instead of one of them is more biologically reliable because the interaction between the two variables. The AGR was supposed as the more "effective, comprehensive, and potential biomarker" for the prognosis of cancer patients due to its easy access and little cost in clinical practice.[33] Diverse studies have notified the relationship between AGR and prognosis in different types of urologic cancers.[34-37] Liu *et al*.[35] estimated AGR in patients with gastric cancer and confirmed that AGR was an independent predictive marker of valuation in gastric patients. Liu *et al*.[36] measured the AGR in patients with heart failure and found that the increase in the levels of AGR indicated a favorable overall survival. The correlation study indicated that for patients with "uterus and ovary" cancer could use the correlation between (TP with Alb and TP with Glo), while for breast cancer patients could use (TP with Glo and Alb with Glo) to follow the disease.

Conclusion

The ratio of Alb/Glo was significantly decreased in all patients group except patients with breast cancer who showed significant increase compared to healthy participants which could be used in the diagnosis of these patients.

Ethical clearance

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. The study protocol and the subject information and consent form were reviewed and approved by a Local Ethics Committee.

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Conflicts of interest

There are no conflicts of interest.

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