Alteration of Serum Immunoglobulin Levels in Woman with Ovarian Cancer

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Abstract

Ovarian cancer has a high mortality and delayed diagnosis. Several immunological alterations take place during ovarian carcinogenesis, and can be of value in the surveillance of the diseases. This research was conducted to evaluate serum immunoglobulin levels in women with ovarian cancer and to assess their role in disease process. The present study is composed of 85 women (mean age = 62.03±12.4 yrs) with clinically and pathologically confirmed ovarian cancer and 65 healthy females as a control group (mean age = 61±12.1 yrs). ELISA test was achieved for the determination of serum [IgG, IgA, IgM]. The findings of current study illustrated significant (P=0.001) increase in serum IgG, IgA, and IgM levels as compared to controls. Analyzing serum immunoglobulins levels might assist in identifying patients with a weak prediction, the elevation of serum immunoglobulins can be considered as an indication for disease status.

Key words: Ovarian cancer, Immunoglobulin.

Introduction

Ovarian carcinoma is one of the most common malignancy in woman [1]. It has been called a hushed murder, since many Ovarian carcinoma are symptomless in the untimely grade and so do not appears until the disease is at a proceed grade. Most women with Ovarian carcinoma are, therefore, identified and diagnosed with late stage of carcinoma [2]

Ovarian carcinoma has the highest death rate in cancer of a woman's reproductive organs at present [3]. Due to the absence of typical Clinical manifestations at creation grade, most patients with Ovarian carcinoma have get to a proceed grade by the time the detection is established, and even some have previously Spread throughout the body [4]. Clinically, Ovarian carcinoma is mainly healed up by removing tumors from patients with peritoneal mesothelioma and Adjuvant chemotherapy in order to prevent recurrence of the tumors, particularly distant recurrence. However, for patients at a proceed grade and with a metastatic growth [5, 6].

Immunoglobulins play a key role in the maintenance immunity of human body's immune system; polypeptide chains of immunoglobulins are classified into four chains: two "light" chains and two "heavy" chains. Isotypes of immunoglobulin which included (immunoglobulins A(IgA), immunoglobulins D(IgD), immunoglobulins G(IgG), immunoglobulins E(IgE), and immunoglobulins M (IgM), respectively are assessed by the kind of heavy chain [7].

However, some previous studies have recorded that immunoglobulins were observed to be expressed in various malignant epithelium cancer and activated in the enlargement of epithelium, but it was inversely expressed in normal epithelial cells [8, 9].

Heavy polypeptide chains and light polypeptide chains constant zone of immunoglobulin was present in a number of epithelial carcinoma cell lines, like (human breast cancer cell line), (human colorectal cancer cell line), (human stomach cancer cell line), a (human neck cancer cell line), and (Nasopharyngeal cancer cell line) [10]. Furthermore, some human carcinoma cell lines could release immunoglobulins G [11,12] and immunoglobulins G and immunoglobulins A were also observed to be expressed in cancer of oral epithelial by immunohistochemical analysis which based on antibodies binding specifically to antigens in biological tissues to detect the antigens (e.g.proteins) [13]. The earlier classic understanding that immunoglobulins were produced only by B lymphocytes and plasma cells were challenged when many non-lymphoid lineage cells such cancer cells were observed to have the capacity to form immunoglobulins G [14]. Earlier, potential defect in the secretion of immunoglobulins causes disturbance in the metabolic pathway of immunoglobulin has been proposed in the mechanisms of various carcinoma. Circulating immunoglobulins concentrations were found to be linked to cancer grade and tumour mass in carcinoma such as neck carcinoma, cancer of pancreas carcinoma, primary hepatic carcinoma [15] and cancer of skin cell [16]. In patients with oral carcinoma, Earlier examination of circulating immunoglobulin concentrations revealed an elevate in immunoglobulins M, immunoglobulins A, immunoglobulins E, and immunoglobulins G in comparison to healthy peoples [17].

Previous studies[18] refuted the prior finding and found that circulating immunoglobulins concentrations G and immunoglobulins A levels are not remarkably increased in oral carcinoma and therefore not to be utilized as a best alternative indicator for detection and prognosis. The goal of current study is to assess the immunological response in patients with ovarian carcinoma as a biochemical marker in prediction and therapy response indicators.

Methods and Materials

Subjects

The present study included 85 woman, aged 29–70 years, who were visited the Hiwa Hospital in Sulaymaniyah. These females were diagnosed to have ovarian carcinoma. A total of 65 apparently healthy female without any history of ovarian carcinoma were included in the present study as a control group. Ethical approval and permission for the study was taken from the Ethical Committee of Sulaymaniyah University (Iraq). Informed consent was taken from all the study subjects purely for research purpose.

Samples

Collection of the blood

Blood was sampled before any treatment was given**.** Six milliliters of venous blood were taken without using tornique from each individual, collected in plane polyethylene tube, allowed to stand at room temperature for thirty minutes, then the sample was centrifuged at (2000xg) for 10 minutes, the obtained serum transferred immediately to another test tube. These samples were estimated directly for enzymes activities or frozen at – 20 C for subsequent analysis.

Methods

Assay of serum immunoglobulin (IgG, IgA, and IgM)

Serum immunoglobulin levels were measured using a quantitative sandwich enzyme-linked immunosorbent assay according to the kit procedure.

Principle of assay

This ELISA kit uses Sandwich-ELISA as the method. The Microelisa stripplate provided in this kit has been pre-coated with an antibody specific to Ig. Standards or samples are added to the appropriate Microelisa stripplate wells and combined to the specific antibody. Then a Horseradish Peroxidase (HRP)-conjugated antibody specific for Ig is added to each Microelisa stripplate well and incubated. Free components (unbound conjugated antibodies) are washed away.

The 3,3',5,5'-tetramethylbenzidine (TMB) substrate solution is added to each well. Only those wells that contain IL-6 and HRP-conjugated Ig antibody will appear blue in color and then turn yellow after the addition of the stop solution (0.16M H_2SO_4). The optical density (OD) is measured spectrophotometrically at a wavelength of 450 nm. The OD value is directly proportional to the concentration of IL-6 in standards and samples. We can calculate the concentration of Ig in the samples by comparing the OD of the samples to the standard curve.

Statistical analysis

Statistical analysis was performed using the software Statistical Package for Social Sciences (SPSS) including data evaluation and tests for significance. Graph plots were done via windows excel version.

Results and Discussion

Figures (1,2,3) shows the results of Serum Immunoglobulins (IgG, IgA, and IgM) levels in samples of control and ovarian cancer patients. The results reflect a significant increase ((P=0.001)) in the levels of (IgG, IgA, and IgM) in ovarian cancer patient groups in comparison to that of the control,
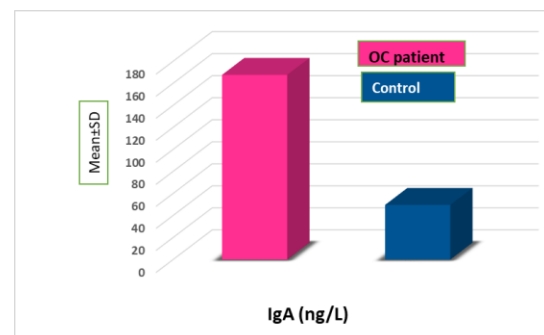

Figure 1. Mean values of serum Immunoglobulin A (IgA) levels in control and Ovarian cancer patients .
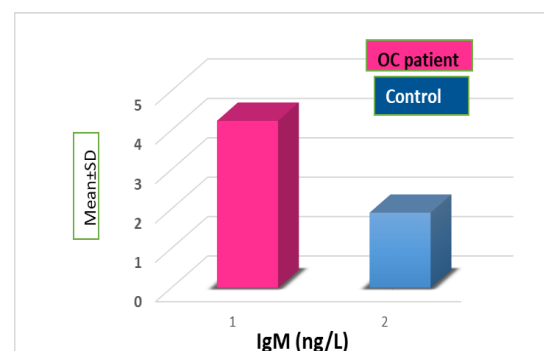

Figure 2. Mean values of serum Immunoglobulin M (IgM) levels in control and Ovarian cancer patients
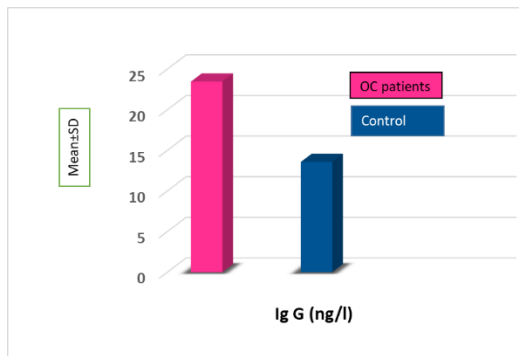
Figure 3. Mean values of serum Immunoglobulin G (IgG) levels in control and Ovarian cancer patients

The capacity to intercede and escalate the effect of the immune system to create a helpful anticancer reaction remains an area of extensive study. The progression of carcinoma may suggest a failure in the immune reactions, like mechanism of tumor get away. Cancer cells show a different mechanism that makes them to control detection of the immune system and demolition, enabling the responsivity of immune system unsuccessful. Throughout the progression of cancer, the capacity of the human immune system to detect and demolish developing cancer cell and as a result to act as a primary protection versus tumor has been considered for many decades. Various reports now provide engrossing confirmation that specific immune response types, selectivelatory and regulatory molecules, and tracks can sometimes completely act as extraneous tumor inhibitor mechanisms [19] and hence, throughout cancer prognostication, circulating concentration of immunoglobulins are changed significantly to recompense for the altering surroundings of the carcinoma cell. Levels of immune complexes are perceptible in patients with cancer of the head and neck, gastric, rectum, lungs, and in patients with malignant tumors [20]

The reproducible elevation of sera IgA and IgG of breast cancer patients observed in this study, may be a result of the natural antibody response to the presence of antigens of breast cancer, or as a defense reaction against increasing tumor load, or may be due to the secretion of immunoglobulin by the tumor itself [21, 22]. The current study is in line with that of [23].

Assessment of serum immunoglobulin levels in human carcinoma has been recorded by a numbers of investigators such as cancer of neck, pancreatic carcinoma [24], skin carcinoma [25] and breast carcinoma [26, 27], with altered results and thinking .

In patients with oral cancer, previous researchers of circulating immunoglobulin levels demonstrate an elevate in IgM, IgA, Ig E, and IgG when compared with normal peoples. Previous studies go against the prior results and found that circulating IgG and IgA are increased remarkably in oral carcinoma and to be utilized as a best alternative indicator for detection and prognosis. Elevated concentrations of immunoglobulin M in cancer patients have been observed to associate with the clinical grades. On the contradictory a study from India [28] reported no remarkable elevate in immunoglobulin M concentrations with development of cancer.

Various reactions of immune defects have been linked with cancer cell and immunoglobulins are synthesized not only by B cells and cells of plasma but by other nonlymphoid lineage cells like malignant tumor. This describe the action of immune disturbance in the metabolic pathway of immunoglobulin and mechanism of ovarian carcinoma. Expression of several types of immunoglobulins has been observed to associate with malignancy [29, 30] and may be correlate with formation, progression and diagnosis of the carcinoma cell as explained and identified by the American Joint Committee on Cancer. Significant elevate in immunoglobulin M was reported in breast fluid in women with breast cancer before surgery to remove all cancer tissue with diminish in immunoglobulin A and in immunoglobulin G concentrations and in immunoglobulin G concentrations found to associate with infiltration in plasma cell.

Conclusions

The findings of the present study suggest that the elevated levels of serum immunoglobulins (IgG, IgM and IgA) can be considered as useful biomarker in diagnosis patients with ovarian carcinoma, and alteration of circulating immunoglobulins (IgG, IgM and IgA) levels are strongly associated with ovarian carcinoma.

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