J.Thi-Qar Sci. Vol.2 (3) Spt./2010

ISSN 1991- 8690 الترقيم الدولي ١٩٩١ - ٨٦٩٠

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# Evaluation of complement components C3 and C4 in serum of patient with neoplastic diseases

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## Abstract

The aim of this study is to evaluate the level of complement components C3 and C4 in serum of cancer patients to find which activation pathway of the complment system has the more effect in these cases . A total of 20 blood samples were collected from cancer patients , C3 and C4 complement components were measured by SRID plates . The results showed a significant elevation in $C_3$ and $C_4$ level in compartion with control group. C3 level was higher than C4 level which suggest that the activation of classical pathway in cancer patients .

## Introduction:

Cancer is a synonym for malignant disease or neoplasm (Brandwald *et al.*, 2001) , cancer cells lose the functional and phenotypic characteristics of the tissue from which they are derived and said to have undergone malignant transformation and to be de-differentiated . Some malignancies are capable of breaking up and spreading via the circulatory or lymphatic system to remote sites . as a result new foci of malignant cell growth (metastasis) are established far removed from the original tissue in which the cancer developed.(Eales,1996).

The existence of the immune response against a tumor is based in the surface components of the malignant cell that don't occur in its normal contour part that give rise to structures that are antigenic (Benjamini *et al.*, 2000) .The first line of defense is the innate immunity including the complement system, which is the name given to a complex series of 20 proteins found in plasma, this system characteristically produce a rapid, highly amplified response to a trigger stimulus mediated by a cascade phenomenon where the product of one reaction is enzymatic catalyst the next (Roitt ,1998). In the sera of patients with neoplasia there often occur significant variations in the levels of complement or of their single components (Weimer, *et al.*,1964). In general, it has been observed that complement is increased in the serum with the spread of the disease ( Nishioka,

*et al.*, 1976). The biological significance of the fluctuation is still not clear ( Carli, *et.al.*,1979) . Complement activated by three ways , the classical pathway, lectinpathway (mannose-binding lectin MBL) and the alternative pathway ,the most abundant and the most pivotal component are C3 which its concentration in plasma is 1200 µg \ml with a molecular weight 185000 dalton and associated with the classical ,MBL and alternative pathways , and C4 which its concentration in plasma is 640 µg \ml with a molecular weight 20000 dalton and associated with only the classical and MBL pathways of activation (Benjamini *et al.*, 2000).

The aim of this study is to compare both C3 and C4 levels in patients with different types of cancer in order to detect which activation pathway is the most effective.

## Materials and Methods :

Blood samples were collected from patients seen in the Oncology Center in Basrah and healthy people . These samples divided into 2 groups ,the first group was patients with different types of malignancy (20 samples ) , the second was the control group (4 samples).The serum separated into , 5 µl added in C3 and C4 Single Radial Immunodiffusion (SRID) plate's wells , then incubated at 23 $C^o$ for 48 h. after that the diameter of the precipitation measured with a suitable lens then the results were evaluated using the table of reference . Statistics analysis performed by ANOVA test.

## Results and Discussion :

Patients with neoplasia distributed as shown in table 1 :

Table 1 : Types and number of neoplasia

| Type of neoplasia | Acute lymphatic leukemia(ALL) | Acute Myeloid Leukemia (AML) | Non–Hodgkin lymphoma (NHL) | Breast cancer | Stomach cancer | Sarcoma* |
|---|---|---|---|---|---|---|
| Number | 8 | 1 | 2 | 1 | 1 | 7 |

The results showed a significant elevation in $C_3$ and $C_4$ level in cancer patients in compared with healthy people ($P>0.05$) , $C_3$ mean value was 123.15

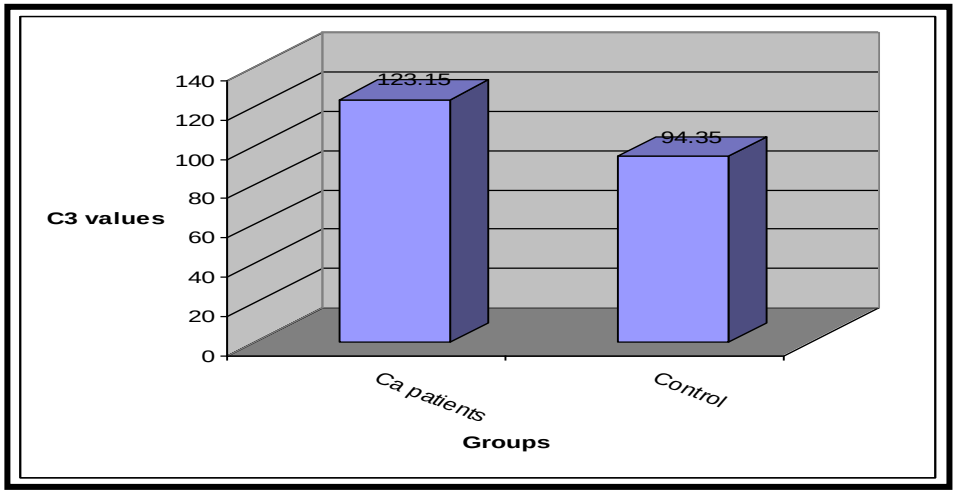
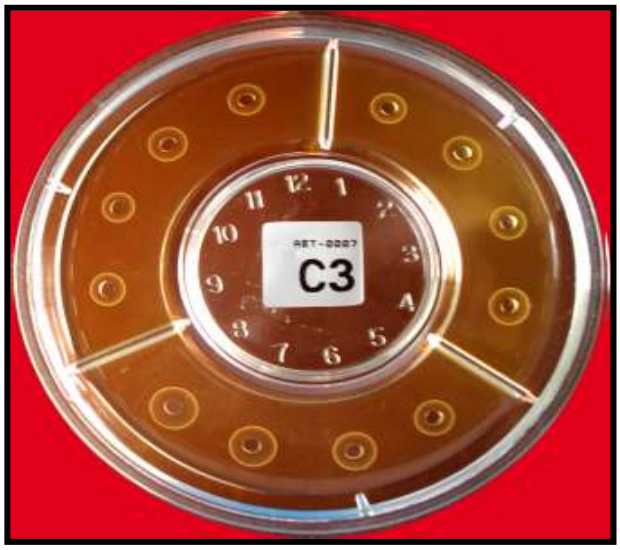



Figure (1): The complement component $C_3$ mean value in cancer and healthy






Picture (1): precipitation rings of $C_3$ in SRID test


Picture (1): precipitation rings of $C_4$ in SRID test

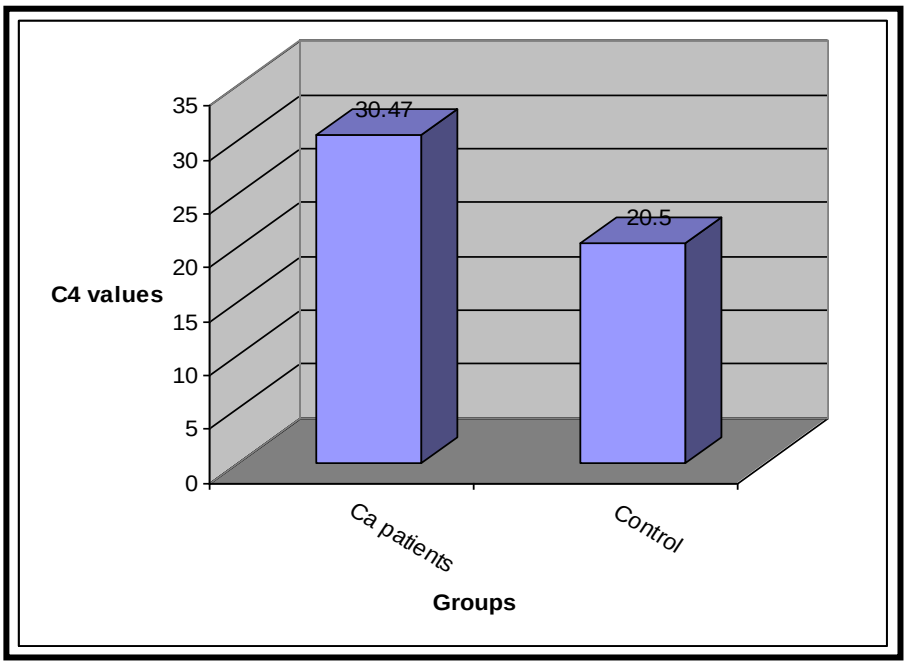



Figure (2): the complement component $C_4$ mean value in cancer and healthy people

## Conclusion :

Tumor cell antigens often elicite the production of specific serum antibodies .These antibodies can play a protective role in elimination of the tumor through several mechanisms .In some cases the antibody can activate the complement system ,leading to assembly of the membrane attack complex (MAC), pore formation and complement mediated lysis .Some tumors however have been

shown to endocytose the MAC pore and repair the membrane before the cell is lysed .In these cases complement split products such as C3a ,C4a,C5a and C5b67 can still play a significant role by inducing localized mast cells degranulation and release of mediators that facilitates the in flux of inflammotary cells ,especially neutrophils and macrophages. (Kuby,1993).

It could be said that this elevation of C3 and C4 is an ordinary results because of the role of complement as an immune response to the cancer. Our results and those of Carli, *et al.* (1979) and Verhaegen , *et al.*(1976) demonstrate a significantly elevated complement levels in patients with neoplastic disease compared with healthy people, Perhaps the elevated complement level in these patients serves to compensate for the diminished reaction capacity of the cellular immune system, which defends the host against the tumor.(Carli, *et al.*, 1979 ) 'The high complement levels in neoplastic disease may be caused by the continued presence of a tumor mass, which serves as an antigenic-stimulus for continued antibody production. The antigen-antibody complexes require complement which causes an increased production to maintain normal levels. It might well be that this increased production has a rebound effect, whereby sustained high complement levels are produced (Verhaegen , *et al.*,1976).

Both IgM and IgG antibodies have been shown to destroy tumor cells in vitro in the presence of complement .Several studies conducted with mice indicate that, in the presence of complement ,antitumor antibodies are effective in destroying some leukaemia and lymphoma cells and in reducing metastasis in several other tumor systems (Benjamini, *et al.*,2000).

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# تقييم مستوى مكوني المتمم C3 و C4 في مصول المرضى المصابين بالسرطان

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## الخلاصة

الهدف من الدراسة هو تقييم لمستوى مكوني المتمم C3 و C4 في مصول المرضى المصابين بانواع مختلفة من السرطانات و تقييم أي من طرق التنشيط الخاصة بالمتمم هي اكثر فاعلية . و تضمنت الدراسة جمع ٢٠ عينة دم من المرضى و قياس مستوى مكوني المتمم C3 و C4 باستخدام اطباق الانتشار المناعي القطري البسيط SRID . أظهرت النتائج ارتفاع معنوياً لكلا المكونين بالمقارنة مع مجموعة السيطرة و كان المكون C3 هو اعلى مستوى من المكون C4 و هذا يقترح ان تنشيط المتمم بالطريقة الكلاسيكية تُفعّل اكثر من طرق التنشيط الاخرى في مرضى السرطان .