# Immunoglobulins Levels and Complements in Patients with Brain Tumour (Meningioma and Glioma)

مستوى الكلوبيولينات المناعية والعامل المكمل للمرضى المصابين باورام الدماغ

( الاورام السحائية واورام الخلايا الدبقة)

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المستخلص:

**الهدف:** تهدف الدراسة الحالية الى دراسة العلاقة بين الكلوبيولينات المناعية IgG, IgA, IgM فضلا عن العامل المكمل C3 و C4 لمناعة المرضى المصابين باورام الدماغ ( الاورام السحائية واورام الخلايا الدبقة) .

**المنهجية:** اربعون عينة دم من المرضى المصابين باورام الدماغ تضمنت ٢٠ عينة لاورام الخلايا الدبقة و ٢٠ عينة للاورام السحائية تم اختبار المصل لتحديد مستوى الكلوبيولينات المناعية IgG, IgA, IgM والعامل المكمل C3 و C4 باستخدام تقنية الانتشار المناعي الحلقي المفرد وتم مقارنتهم مع اشخاص اصحاء ظاهريا

**النتائج:** أظهرت الدراسة الحالية انخفاض معنوي لمستوى IgG في عينات اورام الخلايا الدبقة عند مقارنتها مع عينات الاورام السحائية ومجموعة السيطرة. مستوى الكلوبيولينات الاخرى والعامل المكمل لكلا النوعين من الاورام اظهرت فروقا غير معنوية عند مقارنتها مع مجموعة الاشخاص الاصحاء ظاهريا.

**التوصيات:** توصي الدراسة باستخدام تحاليل اخرى مصلية او نسيجية على المستوى الجزيئي لانواع اخرى من اورام الدماغ ولمراحل مختلفة من تطور المرض

**Abstract:**

Objective: The present study aims at studying the relationship between immunoglobulin IgG, IgA, IgM , as well as to C-3 and C-4 in brain tumours patients immunity (meningioms and gliomas).

**Methodology**: Forty sera of brain tumour patients were included 20 glioma and 20 meningioma was tested to determine the levels of IgM, IgG IgA, C-3 and C-4 by using single radial immune-diffusion technique and compared with 20 apparently healthy blood donors.

**Results**: The study revealed a significant decreasing in IgG levels in glioma as compare to meningioma and control. The concentration of two other serum immunoglobulins and complement in both meningioma and glioma show no significant differences with those in control group.

**Recommendations**: The study recommends using serum and tissues in molecular level in other type of brain tumour with different grades.

**Key Words: Brain Tumour , Meningioma, Glioma, Immunoglobulins, Complement.**

## Introduction

Brain tumour is an abnormal growth of tissue in the central spin or brain that can effect in normal brain action. Numerous types of brain tumours exist, some are noncancerous (benign), and some are cancerous (malignant). Brain tumours can take place in the brain (primary brain tumours), or from other parts of the body and reach to the brain (secondary, or metastatic, brain tumours) [1].

Immune-globulins are proteins generate by plasma cells and lymphocytes. They play an essential part in the body's immune system to recognized and neutralize pathogens such as viruses and bacteria. The antibody recognizes a unique molecule of the harmful agents, called an antigens [2]. It has been supposed that the production of immunoglobulin (Ig) molecules is restricted to B-cells, but numerous studies were found that immunoglobulin genes and proteins in a variety of cancer cells types [3].It has been found that other types of non-hematopoietic cells, especially cancer cells could also produce IgG, and the IgG is involved in the cell survival and carcinogenesis [4].The use of immune-stimulatory antibodies showed great promise in stimulating adaptive immune responses in tumour patients [5].

Complement has an important role in the innate immune system, providing a highly effective in destruction of infesting pathogens, dispose of immune complexes, disposing of dead and dead cells and contributes to the destruction of tumour cells [6], by raised the ability of the malignant cells to stimulate complement proteins [7], and opsonize harmful microorganisms as well as facilitate their clearance by phagocytes, enhance antibody-dependent cellular cytotoxicity, and can lead to the direct lyses of certain species of bacteria. However, the complement activities are highly effective in eliminating infection; they can't reduce the growth of malignant tumours [8].

Malignant cells have used a protective mechanism to inhibit complement activation and avoiding complement-mediated sweeping and restrain the clinical efficiency of antibody cancer immune-therapies [7]. The failure of complement to destroy tumour cells might possibly due to their impedance to complement raid; including lysis mediated by complement [9]. This impedance can result from different techniques, through the expression of membrane complement regulatory proteins (mCRP) [10], which naturally save host cells from destruction by complement and the excretion of soluble complement restrainers,

by tumour cells [11]. Others postulated that the inflammatory effects of complement may actually keep established tumours and induce their growth [12]. In fact, complement has been display an important role in modulating the anti-tumour activity of many m-Ab through complement-dependent cytotoxicity (CDC), antibody-dependent cytotoxicity (ADCC), and through indirect effects by adjusted the tumour microenvironment [13].

## Methodology

### A. Collection of samples

Forty sera from brain tumour patients from specialized surgical hospital and neurological disorders hospital in Baghdad for a surgical resects brain tumour before radiotherapy or chemotherapy treatment. These include 20 glioma and 20 meningioma and compared with 20 apparently healthy subjects.

### B- Single radial immunodiffusion assay (SRID)

The (SRID) test is performed by using LTA Milano kit. The plates were opened and left at room temperature (27 °C) for a few minutes to allow any condensed water in the wells to evaporate. The wells were filled with 5μl of testing sera (patients and control). Then we left a plate to stay at room temperature closed the plat and place it

in a moist chamber for about (48) hour in the case of IgG, IgA, C3 and C4 and for (72) hour in the case of IgM.

### C. Statistical data analysis

The data was statistically analyzed by computer programme SPSS (Statistical Package for Social Sciences) version 13. Their data were given in terms of means ± standard errors (S.E.), and differences between means were estimated by ANOVA tests. The difference was considered significant when the probability (P) value was ≤ 0.05-0.001.

## Results

**Table (1): Immunoglobulins** (IgG, IgA, IgM) **Levels in Sera of Brain Tumour Patients and Control Group**

| Patient Groups | | IgG mg/dl | IgM mg/dl | IgA mg/dl |
|---|---|---|---|---|
| Glioma N = 15 | Mean ± SE | 888.34 ± 41.81 | 302.92 ± 37.06 | 202.89 ± 26.70 |
| | Minimum – Maximum | 701.30 – 1257.10 | 84.90 – 490 | 115.10 – 427.40 |
| | Significant | P< 0.001 | NS. | NS. |
| Meningioma N=15 | Mean ± SE | 1400.88 ±115.85 | 321.94 ± 33.60 | 270.18 ± 41.56 |
| | Minimum – Maximum | 773.40 – 2147.50 | 106.60 - 490 | 115.10 – 503.40 |
| | Significant | NS. | NS. | NS. |
| Control N=15 | Mean ± SE | 1444.12 ± 135.89 | 255.76 ± 18.53 | 270.82 ± 41.05 |
| | Minimum – Maximum | 810.40 – 2606.70 | 109.90 – 388.90 | 115.10 – 715.70 |
| | Significant | NS. | NS. | NS. |

**N= Number,  NS= not significant , SE = Standard Error**

Serum IgG, IgM and IgA levels in brain tumour patients are shown in (Table-1). Patients with glioma (888.34) showed a significant reduction in IgG (P<0.001) as compare to meningioma (1400.88) and control (1444.12), others indicated that there were no significance differences in immunoglobulin levels between two patients group and control.

**Table (2): Complements (C3 and C4) Levels in Sera of Brain Tumour Patients and   Control Group**

| Groups | | C3 mg/dl | C4 mg/dl |
|---|---|---|---|
| Glioma N = 15 | Mean ± SE | 173.15 ± 5.65 | 37.58 ± 3.63 |
| | Minimum – Maximum | 145.70 – 221.70 | 19.20 – 73.20 |
| | Significant | NS. | NS. |
| Meningioma N=15 | Mean ± SE | 193.53 ± 16.10 | 34.54 ± 4.86 |
| | Minimum – Maximum | 105.20 – 305.80 | 14.90 – 76.90 |
| | Significant | NS. | NS. |
| Control N=15 | Mean ± SE | 180.22 ± 13.73 | 28.10 ± 1.55 |
| | Minimum – Maximum | 120.80 – 299.60 | 19.20 – 37.80 |
| | Significant | NS. | NS. |

M = Mean : SD = Standard Deviation

No statistical differences were found in serum level of C3 and C4 patients meningioma and glioma when compared with control Table (2).

## Discussion

Immunoglobulins known to be served as prototypical effector molecules of immune defense against pathogens and cancer cells [3.] The present study indicated that there is no significant difference in IgM and IgA levels. IgG showed a significant reduction in patient with glioma as compared with patients with meningioma and control groups. [14] Were assured that downregulation of IgG limited the growth and proliferation of cancer cells *in vitro* and *in vivo*. Their finding is conversely with the results of [15] in different brain tumour types. [17] Showed positive expression of IgG in glioma patients. The IgG was associated with tumour grade and decreased in malignant tumours compared with benign tumours. A study has reported a significant increase in IgG in benign and malignant brain tumours [15]. Others reported that human tumour cells including cancers of colon, esophagus, thyroid and placental trophablast, breast, lung, prostate, and sarcomas can synthesize immune-globulins such as (IgG) [17]. The level of IgG may associate with the histopathological grading [18]. Immune-globulins such as IgG and IgM have been shown to induce anti tumour cytotoxic activity via CDC or ADCC as mediated by complement or immune effector cells like macrophage natural killer cells [19].

According to the relationship among the immune surveillance, microbial protection and complement has long been supposed to play an effective and important role in fighting against cancer cells. [8] Found that complement proteins C3, C4, and C5a may assist tumour growth through immune-suppression. Notably, complement proteins are direct and indirect participants in angiogenesis [20]. Others report that radiotherapy induced tumour cell death and transiently activated complement both in murine and human tumours [7].

There was no significant difference in the two complement C3 and C4 in patients groups and control groups, but, a contrary results have found an activation and increment of complement system in tumours and in the sera of patients with neoplastic diseases [7]. Serum concentration of the classical, lectin and alternative complement pathways are significantly altered in glial tumour patients, suggesting the relationship between the innate immune system in glial tumour pathology [21]. Complement able help the escape of tumour cells from immune-surveillance, activate mitogenic signaling pathways, enhance angiogenesis, support cellular generation and resistance to apoptosis, and collaborating in tumour cell

attack and infiltration [22]. The conflict results my due to the small sample size or different tumour types and stages.

**Recommendations**

The study recommends using serum and tissues in molecular level in other type of brain tumour with different grades.

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