

Study the Levels of IL-12 and Alkaline Phosphatase in Brain Tumor Patients

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Abstract

Current study aimed to accomplished by assessment levels of alkaline phosphatase and IL-12 levels in Iraqi patients with brain tumor. From November 2021 to February 2022, researchers at Al-Hussein Hospital in Karbala, Iraq, will investigate the prevalence of bacteremia and immunological markers in patients with brain tumors. 50 patients with brain tumors (27 males, 23 females) and 30 healthy people as control both patients and controls had blood drawn. Interleukin-12 (IL-12) levels estimated by ELISA technique. The findings indicated that the most vulnerable age group was 1–10-year-old, with a 26% infection rate compared to other age groups. Interleukin-12 levels in patients were lower than in healthy controls, while the level of Alkaline Phosphatase (188.22 U/L) was not substantially different from the healthy (187.76 U/L). Its conclude there's no significant difference in the level of alkaline phosphatase in patients than in healthy; so IL-12, It has been found the level has decreased in patients than in healthy persons.

Keywords: Brain, Alkaline phosphatase, IL-12, tumor.

1. Introduction

As predicted, the human brain has the same number of neurons as a monkey brain of comparable size (Marino et al. 2007). More than 80 percent of brain mass is ascribed to an overdeveloped cerebral cortex that contains 100 billion neurons and ten times as many glial cells. Countless neurons and non-neuronal cells were discovered therein (Herculano-Houzel 2009). When cells multiply and replicate uncontrollably in an intracranial tumor, commonly known as a brain tumor, they seem to be unchecked by the regular mechanisms that regulate cells. Primary and metastatic brain tumors are the two most frequent forms; however, there are more than 150 other varieties. As a general rule, primary brain tumors grow from inside the brain's tissues or its immediate surroundings. Primary tumors in the brain, whether glial or non-glial (forming on or in the brain's nerves, blood vessels, or glands), are either benign or malignant. Metastatic brain tumors are cancers that originate elsewhere in the body (such as the breast or lungs) and then spread to the brain through the circulatory system. Cancerous tumors that have spread to other parts of the body are known as metastatic tumors (Wang et al. 2020).

Malignant tumors in these patients are linked to the development and progression of interleukin (IL)-12, for example. IL-12 is considered a potential cancer immunotherapy approach due to its strong effect on the establishment of an anticancer immune response. IL-12 has been shown in multiple studies to successfully kill cancer cells both in vitro and in vivo. Tumor-associated macrophages' tumor-supportive activities may be drastically reduced by IL-12's antiangiogenic

and antiangiogenic properties (Hong et al. 2022). Alkaline phosphatase (EC3. 1.3.1.) is an enzyme that breaks down phosphate monoesters in acidic environments. Intestinal ALP, Placental ALP, Germ cell 2 ALP, and tissue nonspecific (L/B/K) ALP are the four isozymes of alkaline phosphatase based on where it is expressed in the body. Toward the end of chromosome 2's long arm, it is located (Sharma et al. 2014). Because of the lack of studies on this subject in Iraq, we believe it is necessary to study this pathological condition, which has had an impact on its spread in Iraq over the past two decades.

In this study, immunological changes occur in brain cancer patients were studied and compared with healthy patients. The study's aim is accomplished by assessment levels of alkaline phosphatase and IL-12 levels.

2. Materials and Methods

Blood samples were collected from patients with brain tumor (50 samples and with 30 samples from healthy persons), where the blood sample was withdrawn from patients and healthy persons. Samples have been placed in a gel tube and then centrifugation to obtained serum. The withdrawal of serum and its placement in the Pendroff tubes to be use in biochemical and immunological tests required (Alkaline phosphatase and IL-12) according to procedure that provided with each kit.

3. Statistical Analysis

Chi-square tests were used in the analysis of data from SAS 2012. The results were compared using a less important difference (LSD) at a probability level of 0.05, 0.01. The Data was analyzed in a CRD (Complete Randomized Design) In a practical way

2x2x6. The averages were compared with L.S.D (less important difference) and Chi -square at a probability level of 0.05, 0.01 using S A S 2012. SAS 2012. Statistical Analysis System, User,s Guide. Statistical. Version 9.1st ed. SAS. Institute Incorporated Cary. N.C. USA.

4. Results

he current study included 50 patients (27 male and 23 female) diagnosed by the physician with a brain tumor and these patients reviewed to the Warith International Cancer Institute in the city of Karbala, and 30 persons (12 male and 18 female) as control as shown in [Table 1](#) and [Table 2](#), which represents the number and proportion of patients according to the age group its observed in this study that the category of children aged 1-10 age was the most likely For injury, the rate of infection was 26% compared to the other age groups that were lower than this percentage. Also, through our study, which focused on the study of immune factors mentioned in the proposal, for IL-12, there is no significant difference between the healthy and the patients, but there is a mathematical difference where the level of IL-12 in patients is lower than in the healthy as described in [Table 3](#), [Table 4](#) and [Table 4.6](#) As for Alkaline phosphatase [Figure 4.3](#) and [Figure 4.7](#), which was worth 188.22 (U/L) compared to the healthy 187.76(U/L), which does not indicate a significant difference between patients and the healthy [Figure 4.1](#) and [Figure 4.5](#)

Table (1) Demographic properties of studying groups

Group properties	Number	Sex	Percentage
Patients	50	M 27 F 23	%54% 46
Controls	30	M 12 F 18	%24 %36

Table (2) Age distribution of patients and control

Age group	Number	Percentage
10-1	13	%26
20-10	10	%20
30-20	7	%14
40-30	8	%16
50-40	6	%12
> 50	6	%12
Total	50	100

Table (3) Show concentration of alkaline phosphatase (U/L)

Factor Group	Alkaline phosphatase
Patients	13.96±188.22
Controls	22.52±187.76
P value	n. s

Table (4) Show IL-12 (pg/mL) levels in both groups

Factor Group	IL-12
Patients	4.60 ±21.80
Controls	4.02 ±26.09
P value	n. s

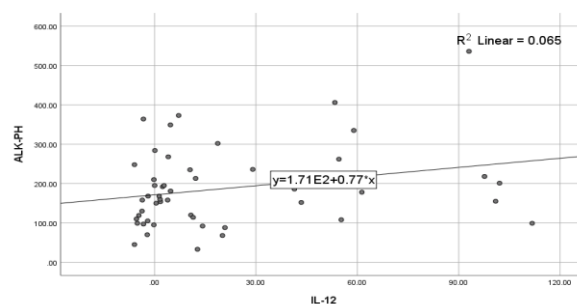


Figure 4.1 The quantitative relationship between the Alkaline phosphatase and IL-12 for patients

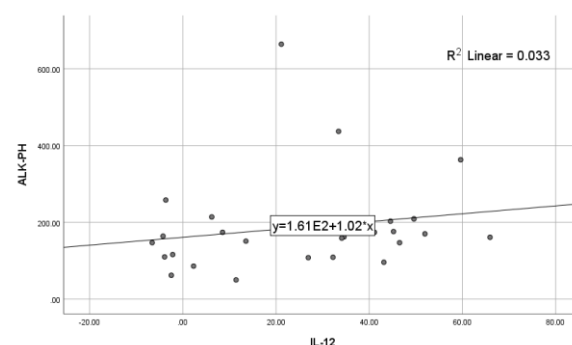


Figure (1) The quantitative relationship between Alkaline phosphatase and IL-12 for healthy persons.

5. Discussion

In our study and through the results obtained it was found that the level of interleukin-12 has decreased, and this indicates that this cytokine has an important role in reducing the spread of the tumor as in healthy people it was more than in patients and therefore it can be noted that this cytokine has a role in the process of the formation and spread of tumor in the human body. It has emerged during the last two decades as one of the most powerful cytokines in preclinical models for promoting anticancer activity. Macrophages, T lymphocytes, and dendritic cells are all impacted by IL-12 in the tumor microenvironment ([Tugues et al. 2015b](#)). The cytokine IL-12 has the potential to greatly increase the anticancer immune response in preclinical studies. Immune responses to tumors caused by IL-12 are modulated by the kinds and locations of tumors, as well as the cytokines and effector cells involved. The delivery of IL-12 to the tumor site for therapeutic reasons necessitates new approaches. This cytokine is produced by APCs like dendritic cells (DCs), macrophages, and B cells when triggered by Toll-like receptors (TLRs). Research by Trinchieri and colleagues, 1993 Because of this, infections trigger the release of the proinflammatory cytokine IL-12. According to ([Medzhitov 2001](#)), Interferon-g (IFN-g), as well as other amplification signals, may be used ([B. X. Ma et al, 1996](#)) IFN-gamma (IL-10) and TGF-b1 (TGF-b1), on the other hand, inhibit the production of IL-12 ([Du and Sriram 1998](#), [Tugues et al. 2015b](#)). Cancer cells have been made to continually secrete IL-12 in order to understand how this cytokine causes antitumor immune responses. TSA breast adenocarcinoma and C26 colon carcinoma cells overexpressed with IL-12 underwent tumor

suppression upon subcutaneous injection (Cavallo *et al.* 1997, Eisenring *et al.* 2010, Martinotti *et al.* 1993). When it came to the rejection of breast cancer TSA-IL-12 cells, IFN-g secreted by CD8 cytotoxic T cells was all that was needed, as opposed to ILCs in B16 melanoma (Cavallo *et al.* 1997). Tumor rejection in the central nervous system has been attributed in large part to T cells that are sensitive to IL-12 (Vetter *et al.* 2009, Berg *et al.* 2013). Tumor cell type and tumor location, as well as certain effector cell types and cytokines, have an impact on the quality of the immune response to tumors, according to these studies. IFN γ -inducible chemokine levels are up, and VEGF and metalloproteinase-9 synthesis are down when IL-12 is inhibiting tumor vasculature formation, according to research (Dias *et al.* 1998, Kanegane *et al.* 1998, Mitola *et al.* 2022).

Studies show that IL-12-induced IFN-g is an important tumor growth inhibitor (Tugues *et al.* 2015b, Cancer and York 2004). Even after tumor injection, IL-12's anticancer effects were still evident, and they were discovered to be partly reliant on CD8 T cells (Tugues *et al.* 2015b).

The supplied IL-12 was shown to activate myeloid cells and promote tumor antigen-specific CD8 T cells, which resulted in tumor regression (Kerkar *et al.* 2011, Lisiero *et al.* 2011, Zhang *et al.* 2009, Pegram *et al.* 2012). IL-12 delivered directly to the tumor site via immunocytokines is a relatively new development. Antibodies specific to the tumor's vascular system or necrotic core DNA have recently been fused with immunocytokines (Halin *et al.* 2002, Somavilla *et al.* 2010), for example. Necrotic areas inside tumors are of special interest because of the lack of circulation and cell death in solid tumors. Before utilizing antibody-targeted cytokines, a detailed evaluation of the tumor setting is necessary since significant avidity and retention to the targeted tissue are required for good therapeutic effects. Researchers found that targeting CD30 lymphoma cells with dual cytokine-antibody fusion proteins reduced tumor growth more efficiently than doing so with simply IL-12 or IL-2 as a single antigen in their treatment regimen.

IL-12 increases IFN production via activating CD8⁺ T cells and NK cells, which in turn increases IFN production. Studies have demonstrated that IFN- γ may kill tumor cells directly, stop the growth of blood vessels, increase the generation of NK cells, CTLs, and macrophages, all while increasing the expression of MHC I and II molecules on the tumor cell's surface. (Bromberg *et al.* 1996, Martini *et al.* 2010, Hayakawa *et al.* 2002, Rosa *et al.* 1986). Systemic injection of therapeutic IL-12, which has shown the ability to ameliorate local immune suppression in preclinical models, has been hampered by substantial inflammation-related adverse effects in clinical studies. To our knowledge, this is the first time that low doses of an antibody fusion protein (NHS-rmIL-12) have been successfully employed to inhibit syngeneic carcinomas with high immunologic activity (Hong *et al.* 2022). IL-12's anti-

cancer properties have been repeatedly shown in preclinical carcinoma models (Noguchi *et al.* 1996, Zaharoff *et al.* 2010, Thomas *et al.* 2000). Clinical studies of IL-12 treating advanced cancer patients have been stymied by substantial adverse effects seen in early trials (Lacy *et al.* 2009, Higano *et al.* 1997, Hong *et al.* 2022). Cancer immunotherapy might benefit greatly from the addition of IL-12.

These cytokines are released by both immunological and malignant cells. The tumor cell cycle is blocked, apoptosis is induced, and tumor cell growth is prevented by treatments focused on the IL-12 family of cytokines. Therapies that target IL-12 family cytokines and immune checkpoint inhibition are synergistic in nature (Deplanque *et al.* 2017, Eckert *et al.* 2017, Mills *et al.* 2019, Guo *et al.* 2017). There is a broad range of AP levels in the blood of different sexes and ages that are considered normal, though (Li *et al.* 2018). Due to the fact that their bones are still developing, children have naturally high amounts of AP. The typical range of abnormal AP levels is used by doctors and researchers instead of a specific figure. The majority of the time, aberrant AP levels indicate that the body's homeostasis is off balance and needs to be addressed. In-depth analysis of clinical samples Total AP enzyme activity, rather than total AP protein content, is measured using AP assays, which are often used in medical laboratories.

Serum AP concentration was shown to be associated with functional outcome in patients with different forms of brain injury, whereas elevated TNAP was found to be negatively associated with cognitive performance (Vardy *et al.* 2012). In individuals with brain tumors, pneumocarcinoma meningitis was more prevalent, and their CSF AP levels were found to be greater than in control patients with epilepsy and stroke (Lampl *et al.* 1990). Patients with non-traumatic cerebral hemorrhages were shown to have elevated liver AP levels (Meythaler *et al.* 1998). Observed that elevated serum AP levels may emphasize the brain-peripheral immunological interactions during stroke and related acute ischemic stroke to liver enzyme production (Muscari *et al.* 2014). Hyperintensities in significant areas of white matter in the brain have been associated to increased AP levels in patients who have had an ischemic stroke (Liu *et al.* 2016). Alkaline Phosphatase Figure 4.3 and Figure 4.7: It has been observed that the determining factor(R²) for the patients 0.06 and for healthy 0.03. which indicates that the effect of alkaline phosphatase at the level of IL-12 was low. Its conclude of current study the category of children with an age of 1-10 years is more likely in brain cancer from other age groups. There's no significant difference in the level of alkaline phosphatase in patients than in healthy. For IL-12, It has been found that his level has decreased in patients than in healthy.

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