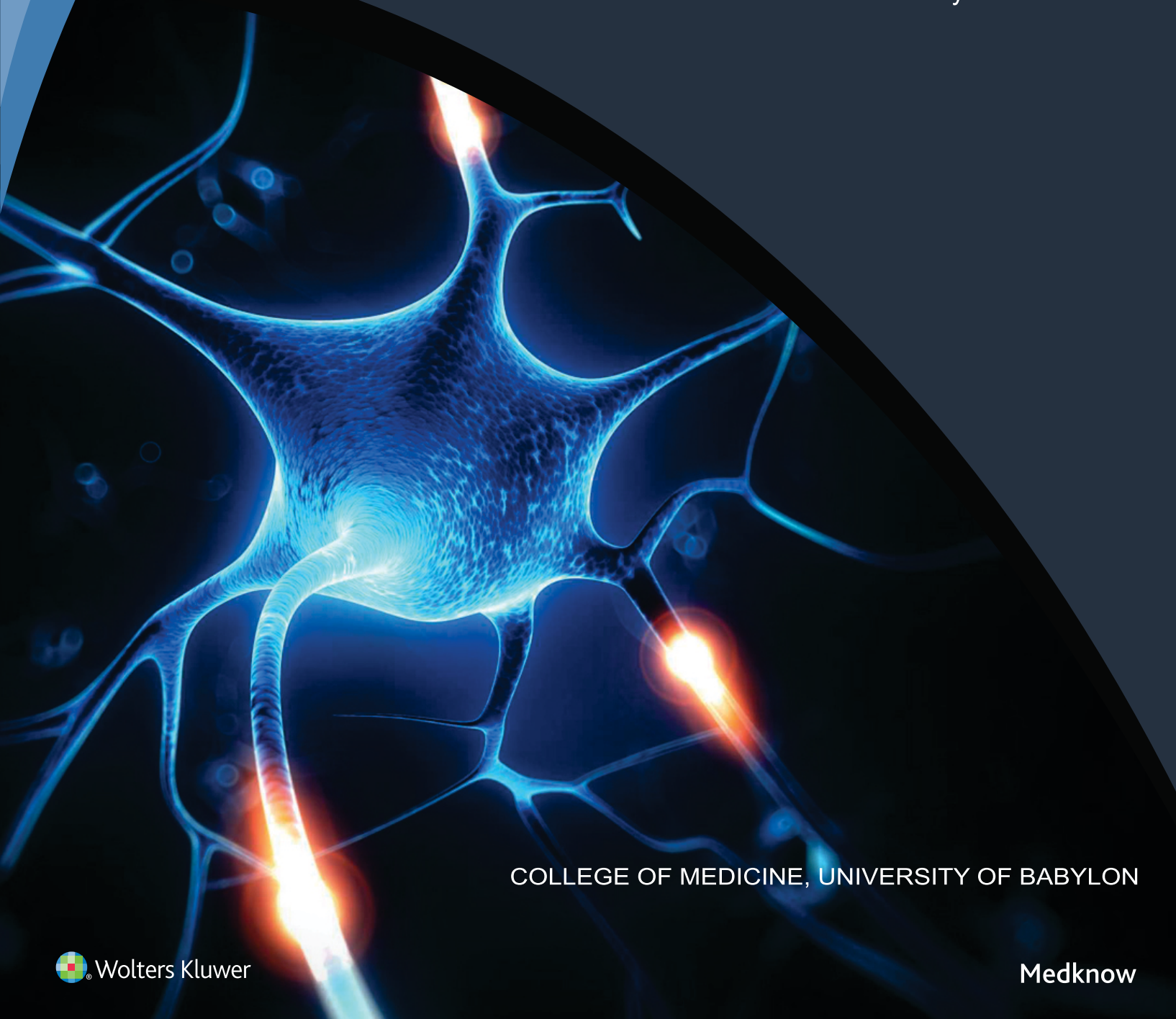


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Cytokines Profile in Patients with Hydatidosis in Babylon Province, Iraq

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Abstract

Background: Hydatidosis is caused by infection with the larval stage of the Cestode *Echinococcus granulosus*. **Objective:** *In vitro* quantitative evaluation of interleukin 6 (IL-6), INF-gamma (INF- γ), and CD4 and CD8 molecules during hydatidosis infection and control group. **Materials and Methods:** *In vitro* quantitative determination of IL-6, INF- γ , and CD4 and CD8 molecules in serum of hydatidosis-infected patients using serological test Sandwich-ELISA. **Results:** The result showed a significant difference in serum IL-6 in patients with hydatidosis than in the control group (38.753 ± 18.307 pg/mL) and 11.752 ± 3.328 , respectively; the differences were highly significant ($P < 0.0001$). The mean of serum CD4 molecules concentration was 5.475 ± 2.335 (ng/mL) and 3.154 ± 1.027 (ng/mL) for controls groups with P value ≤ 0.0001 , while serum concentration of soluble CD8 was 2.977 ± 1.321 (ng/mL) and 1.152 ± 0.699 (ng/mL) for control group with (P value ≤ 0.0001). The ratio of CD4/CD8 was 1.841 in hydatidosis infection patients compared with control group (2.737). **Conclusion:** Immunological parameters included in the present study (IL-6, INF- γ , CD4 and CD8) showed high levels among patients with hydatidosis infection compared to healthy control.

Keywords: CD4, CD8, hydatidosis infection, IL-6, INF-i

INTRODUCTION

Larval infection (hydatid disease, hydatidosis) is characterized by the long-term growth of metacestode (hydatid) cysts in the intermediate host. The two major species of medical and public health importance are *Echinococcus granulosus* and *Echinococcus multilocularis*, which cause cystic echinococcosis (CE).^[1]

Many studies in humans and mice showed that after parasite infections at the beginning dominate T helper 1 (Th1) immune responses. Th1 immune responses are characterized by the release of interferon- γ (IFN- γ) and after priming by dendritic cells (DCs) with IL-12.^[2,3]

Naik *et al.*^[4] detected serum IL-4, IL-10, and IFN- γ of CE patients before and after surgery. The study also found that both Th1 and Th2 cytokine production was present with Th2 predominance at the active stage of disease and a significant decrease of Th2 (IL-4, IL-10) cytokines in patients postsurgery, indicative that IL-4 and IL-10 may

be potential immunological markers for assessing the effectiveness of treatment.

The coexistence of elevated levels of IFN- γ , IL-12, IL-16, IL-18, IL-4, IL-5, IL-10, and IL-13 in most sera of CE patients compared to healthy controls.^[2,5]

Interleukin 6 (IL-6) promotes innate immunity and the elimination of pathogens.^[6]

In addition, IFN- γ is the principal macrophage-activating cytokine and serve a critical function in innate immunity and in specific cell-mediated immunity, it stimulates the expression of major histocompatibility complex (MHC) class 1 and class 2 molecules and stimulates

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antigen-presenting cells, promotes the differentiation of naive CD4 T cells to helper T-cell type 1 (Th1) subset and inhibits the proliferation of Th2.^[7]

Furthermore, CD4 is a glycoprotein coreceptor. It is conveyed on the surface of immune cells, such as T helper cells, macrophages, and DCs. For T cells, 71% are CD4, CD4 mature T-cell spot antigen bind with MHC class II molecules.^[8,9] While CD8 is a trans membrane glycoprotein conveyed as a coreceptor is mainly expressed on the surface of cytotoxic T cells. It is also expressed in natural killer cells and DCs. The CD8 molecule is an indicator of cytotoxic T-cell population. Overall, 29% of T cells are CD8. CD8 mature T-cell recognizes antigen to bind with MHC class I molecules, CD4/CD8 molecules. ELISA test can reveal the percentage of CD4/CD8T cells where flow cytometric instrumentation is unreachable and can be complementary to CD4 T lymphocyte enumeration.^[8]

MATERIALS AND METHODS

Blood collection and storage

“Blood samples were collected by sterile one-use syringes from 33 patients with hydatidosis who were admitted to Al-Hilla Surgical Teaching Hospital and from 25 healthy control, during the period from 20 May to 23 September 2022. Blood samples were permissible to clot for 2 h at room temperature or overnight at 4°C. Sera were separated by centrifugation for 15 min at 1000×g and stored at -20°C.

In vitro quantitative of cytokines and serological markers of cell-mediated immunity

In vitro quantitative determination of IL-6 and INF- γ quantitative determination of IL-6 and INF-rkers of cell-medicecell-mediated immunity in the serum of patients and control groups. IL-6 and INF- γ were detected using Sandwich-ELISA method as in manufacture instructions (Elabscience Biotechnology Co., Ltd, Texas, USA).”

Statistical analysis

The statistical Package for Social Science program version 24.0 (SPSS, IBM Company, Chicago, IL) was used in this study. All values were expressed as mean \pm standard deviation (SD). A *t* test was used to compare between groups.^[10]

Ethical approval

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. It was carried out with patients’ verbal and analytical approval before a sample was taken. The study protocol and the subject information, and consent form were reviewed and approved by a local ethics committee according to the document number 102 on March 28, 2022.

RESULTS

Cytokine profile

According to the results of this study, serum IL-6 was higher in hydatidosis infection patients than in control group (38.753 ± 18.307 pg/mL) and 11.752 ± 3.328 , respectively). The differences were highly significant ($P < 0.0001$; Table 1). INF- γ was higher in hydatidosis patients than in control group (65.27 ± 26.374 and 19.208 ± 6.938 pg/mL), respectively, and the differences were highly significant ($P < 0.0001$; Table 1).

Serum CD4 and CD8

The mean of serum CD4 molecules was 5.475 ± 2.335 (ng/mL) and 3.154 ± 1.027 (ng/mL) for controls groups with P value ≤ 0.0001 , while serum soluble CD8 was 2.977 ± 1.321 (ng/mL) and 1.152 ± 0.699 (ng/mL) for healthy controls with P value ≤ 0.0001 . The ratio of CD4/CD8 was 1.841 in hydatidosis infection patients in compared with control group, which was 2.737 [Table 2].

DISCUSSION

Current data were recorded significant elevation in the concentration of IL-6, INF- γ , and in soluble CD4 and CD8 between hydatidosis patients and control group. Recent findings have shown that CD8 T-cells are capable of secreting IL-10 with or without CD4 T cells and are involved in the regulation of immune response during virus or parasite infection.^[11-13]

IL-6 attenuates the activation of various immuno-competent cells, including neutrophils, monocytes, and macrophages, by limiting the production of proinflammatory cytokines and control the inflammation processes.^[14]

IL-6, promptly and transiently produced in response to infections and tissue injuries, contributes to host defense

Table 1: Concentration of IL-6 and IFN- γ in patients with hydatidosis and control

Cytokines	Group	Concentration (ng/mL) mean \pm SD	P value
IL-6	Patients	* 38.753 ± 18.307	0.0001
	Control	11.752 ± 3.328	
INF- γ	Patients	* 65.27 ± 26.374	0.0001
	Control	19.208 ± 6.938	

* Significant differences $P < 0.0001$

Table 2: Concentration of CD4 and CD8 in patients of hydatidosis and control

Cytokines	Group	Concentration (ng/mL) mean \pm SD	P value
CD4	Patients	* 5.475 ± 2.335	0.0001
	Control	3.154 ± 1.027	
CD8	Patients	* 2.977 ± 1.321	0.0001
	Control	1.152 ± 0.699	

* Significant differences $P \leq 0.0001$

through the stimulation of acute phase responses, hematopoiesis, and immune reactions.^[15] Inflammatory cytokines, such as IL-6 secreted during an infection, may have stimulated erythropoiesis.^[16]

The present study also showed the high mean serum levels of The IFN- γ than control. The promotion in anti-inflammatory cytokine IL-6 in hydatidosis infection combined with elevation in INF- γ concentration within the same group compared with control group.

IFN- γ is a cytokines produced mainly by Th-1 lymphocytes and has many potential activities; its ability to induce the bactericidal activity of macrophages, stimulates the expression of MHC system, and inhibits microbial proliferation.^[17-22]

Cytokines (IL-2, IL-4, IL-6, IFN- γ , and TNF- α) have been shown to be present in serum from hydatidosis infection patients.^[5,23,24]

AL-Masoudi *et al.*^[25] studied the IL-17 cytokine profiles in patients with CE in Babylon Province, Iraq, and they found that there was a significant increase in the serum level concentration of IL17A and IL17B in patients with hydatid disease compared to the control group.

All at once, serum levels of soluble CD4 and CD8 molecules were measured in the current study, and the results showed both CD4 and CD8 molecules were higher in hydatidosis infection patients than control groups, the CD4/CD8 ratio was 1.841 in hydatidosis infection patients in compared to control group which was about 2.737.

CONCLUSIONS

Present work can conclude that there were significant differences in levels of IL-6, INF- γ , and in soluble CD4 and CD8 between hydatidosis infection patients and control group then, cause changing in CD4/CD8 ratio. The results suggest different patterns of activation of Th2 and Th1 cells (according to values of cytokines) depending on clinical status.

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Nil.

Conflicts of interest

There are no conflicts of interest.

Availability of data and material

All data and materials are available upon request.

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