TIBBIYOT
TA'LIMI & INNOVATSIYALARI



- 14.00.00 - Tibbiyot fanlari;
- 14.00.01 - Akusherlik va ginekologiya;
- 14.00.02 - Morfologiya;
- 14.00.03 - Endokrinologiya;
- 14.00.04 - Otorinolaringologiya;
- 14.00.05 - Ichki kasalliklar;
- 14.00.06 - Kardiologiya;
- 14.00.07 - Gigiena;
- 14.00.08 - Oftal'mologiya;
- 14.00.09 - Pediatriya;
- 14.00.10 - Yuqumli kasalliklar;
- 14.00.11 - Dermatologiya va venerologiya;
- 14.00.12 - Tibbiy reabilitologiya;
- 14.00.13 - Nevrologiya;
- 14.00.14 - Onkologiya;
- 14.00.15 - Patologik anatomiya;
- 14.00.16 - Normal va patologik fiziologiya;
- 14.00.17 - Farmakologiya va klinik farmakologiya;
- 14.00.18 - Psixiatriya va narkologiya;
- 14.00.19 - Klinik radiologiya;
- 14.00.20 - Tibbiy genetika;
- 14.00.21 - Stomatologiya;
- 14.00.22 - Travmatologiya va ortopediya;
- 14.00.23 - Hamshiralik ishini tashkil etish;
- 14.00.24 - Sud tibbiyoti;
- 14.00.27 - Xirurgiya;
- 14.00.28 - Neyroxirurgiya;
- 14.00.41 - Xalq tabobati;
- 14.00.35 - Bolalar xirurgiyasi;
- 14.00.34 - Yurak-qon tomir xirurgiyasi

№9-SON

2026-yil, sentabr

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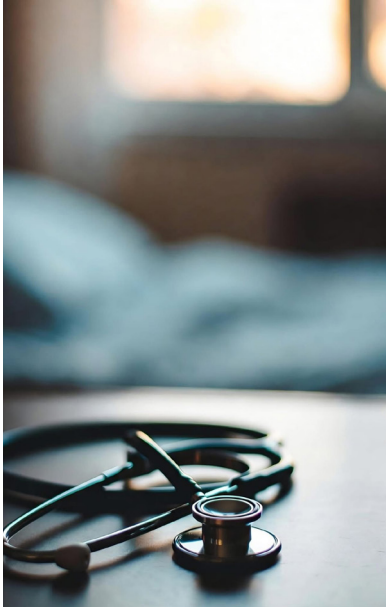





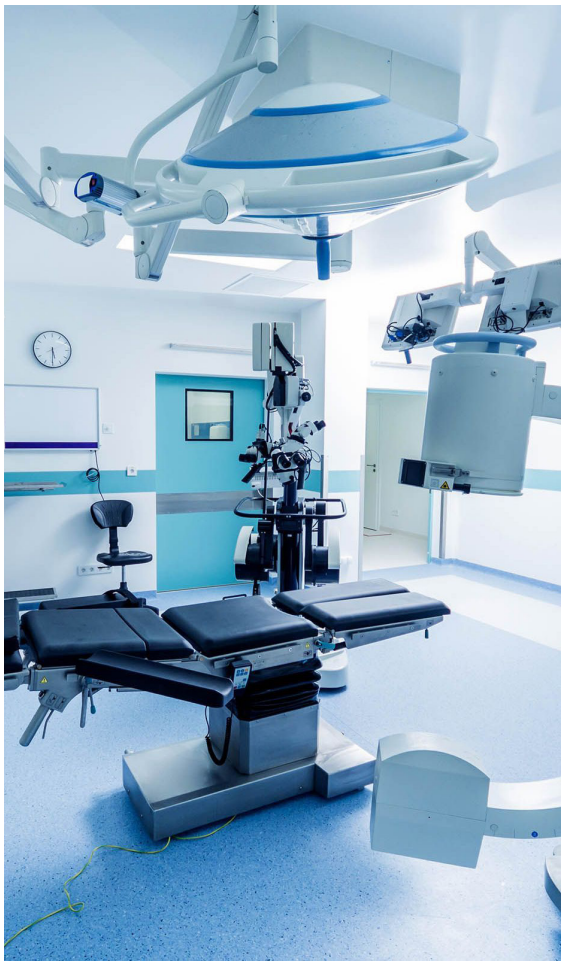



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“Tibbiyot ta'limi va innovasiyalari” ilmi elektron jurnali 29.04.2025-yildan O‘zbekiston Respublikasi Prezidenti Adminstratsiyasi huzuridagi Axborot va ommaviy kommunikatsiyalar agentligi tomonidan C-5669801 reyestr raqami tartibi bo‘yicha ro‘yxatdan o‘tkazilgan. Litsenziya raqami: №745444.

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MUNDARIJA

SEREBROVASKULYAR KASALLIKLARDA BUYRAK SHIKASTLANISHINING ISHEMIK-GIPOKSIK MEXANIZMLARI: HIF-1α VA TGF-β1 KO‘RSATKICHLARINING YOSHGA BOG‘LIQ O‘ZGARISHLARI 16
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RESULTS OF THE STUDY OF CERTAIN CYTOKINES IN PATIENTS WITH THYROID CANCER

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Abstract: The study is devoted to evaluating changes in selected inflammatory cytokines in patients with thyroid cancer before and after treatment and determining their potential clinical significance. The study included 101 patients with thyroid cancer, in whom serum IL-6 and TNF-α concentrations were assessed before and after treatment. Before treatment, IL-6 levels were 8.1 times higher and TNF-α levels were 4.9 times higher than those observed in healthy individuals. Following treatment, IL-6 decreased by 68.0% and TNF-α by 45.8% ($p<0.05$), although both parameters remained significantly above control values. These findings indicate a marked reduction in inflammatory activity after therapy without complete restoration of immunological homeostasis. The authors consider persistent elevation of IL-6 and TNF-α as a potential laboratory manifestation of residual inflammatory activity and an additional indicator of the risk of disease progression. The distinctive approach of the study is the evaluation of cytokine dynamics not only as indicators of systemic inflammation but also as potential markers for monitoring treatment response and subsequent follow-up. The scientific significance of the findings lies in substantiating the potential use of serum IL-6 and TNF-α as additional immunological biomarkers for assessing tumor activity and predicting the course of thyroid cancer.

Key words: thyroid cancer, cytokines, IL-6, TNF-α, antitumor immunity, inflammatory response, immunological biomarkers, treatment monitoring, disease progression.

Annotatsiya: Tadqiqot qalqonsimon bez saratoni bilan kasallangan bemorlarda davolashdan oldin va keyin ayrim yallig‘lanishga oid sitokinlar miqdorining o‘zgarishini baholash hamda ularning klinik ahamiyatini aniqlashga bag‘ishlangan. Tadqiqotga qalqonsimon bez saratoni bilan kasallangan 101 nafar bemor kiritilib, ularda davolashdan oldin va keyin qon zardobidagi IL-6 va TNF-α konsentratsiyalari aniqlangan. Davolashdan oldin IL-6 darajasi sog‘lom shaxslarga nisbatan 8,1 baravar, TNF-α esa 4,9 baravar yuqori bo‘lgan. Davolashdan so‘ng IL-6 miqdori 68,0% ga, TNF-α esa 45,8% ga

kamaygan (p<0,05), biroq har ikkala ko‘rsatkich ham nazorat qiymatlaridan ishonchli darajada yuqoriligicha qolgan. Olingan natijalar terapiya yallig‘lanish reaksiyasining faolligini sezilarli kamaytirishini, ammo immunologik gomeostazning to‘liq tiklanishini ta’minlamasligini ko‘rsatadi. Mualliflar davolashdan keyin IL-6 va TNF-α darajasining yuqori saqlanishini qoldiq yallig‘lanish faolligining ehtimoliy laborator belgisi hamda kasallik progressiyasi xavfining qo‘shimcha ko‘rsatkichi sifatida baholaydilar. Mualliflik yondashuvining o‘ziga xosligi sitokinlar dinamikasini nafaqat tizimli yallig‘lanish ko‘rsatkichi, balki davolash samaradorligini nazorat qilish va bemorlarni keyingi dinamik kuzatish vositasi sifatida baholashdan iborat. Tadqiqotning ilmiy ahamiyati IL-6 va TNF-α ni qalqonsimon bez saratonida o‘sma jarayoni faolligi va kasallik kechishini baholash uchun qo‘shimcha immunologik biomarkerlar sifatida qo‘llash imkoniyatini asoslash bilan belgilanadi.

Kalit so‘zlar: qalqonsimon bez saratoni, sitokinlar, IL-6, TNF-α, o‘smaga qarshi immunitet, yallig‘lanish reaksiyasi, immunologik biomarkerlar, davolash monitoringi, kasallik progressiyasi.

Аннотация: Исследование посвящено оценке изменений отдельных провоспалительных цитокинов у больных раком щитовидной железы до и после лечения и определению их возможного клинического значения. В исследование включен 101 пациент с раком щитовидной железы, у которых определяли сывороточные концентрации ИЛ-6 и ФНО-α до и после проведенной терапии. До начала лечения уровень ИЛ-6 превышал показатели здоровых лиц в 8,1 раза, а ФНО-α — в 4,9 раза. После лечения содержание ИЛ-6 снизилось на 68,0%, а ФНО-α — на 45,8% (p<0,05), однако оба показателя оставались достоверно выше контрольных значений. Полученные результаты свидетельствуют о выраженном уменьшении активности воспалительного ответа под влиянием лечения при отсутствии полного восстановления иммунологического гомеостаза. Авторы рассматривают сохраняющееся повышение ИЛ-6 и ФНО-α как возможный лабораторный признак остаточной воспалительной активности и дополнительный показатель риска прогрессирования заболевания. Особенностью авторского подхода является оценка динамики цитокинов не только как характеристики системного воспаления, но и как потенциального инструмента контроля эффективности терапии и дальнейшего динамического наблюдения. Научная значимость работы заключается в обосновании возможности использования сывороточных ИЛ-6 и ФНО-α в качестве дополнительных иммунологических биомаркеров активности опухолевого процесса и прогнозирования течения рака щитовидной железы.

Ключевые слова: рак щитовидной железы, цитокины, ИЛ-6, ФНО-α, противоопухолевый иммунитет, воспалительная реакция, иммунологические биомаркеры, контроль лечения, прогрессирование заболевания.

INTRODUCTION

Thyroid cancer (TC) is one of the most common malignant tumors of the endocrine system and is characterized by considerable heterogeneity in its clinical course. Although most differentiated forms have a favorable prognosis, some patients develop recurrence and regional or distant metastases, which highlights the need for additional prognostic markers [1,2,5,9]. Current concepts of thyroid carcinogenesis emphasize the important role of immune mechanisms in tumor development and progression. Disorders of innate and adaptive immunity may influence tumor growth, invasion, metastatic potential, and response to treatment [3,4,7,11,12]. Cytokines, particularly interleukin-6 (IL-6) and tumor necrosis factor alpha (TNF-α), are of special interest because they participate in inflammatory and immune responses associated with tumor activity.

The object of the study was the immunological status of patients with thyroid cancer before and after treatment. The subject of the study was the dynamics of serum IL-6 and TNF-α concentrations. The aim of the study was to evaluate changes in IL-6 and TNF-α levels before and after treatment and to determine their potential value as additional immunological biomarkers. The main objectives were to compare cytokine levels with control values, assess their changes after therapy, and evaluate the significance of persistent cytokine elevation for monitoring disease activity and predicting its further course.

LITERATURE REVIEW

Modern studies increasingly consider the immune system as an integral component of thyroid cancer pathogenesis and progression. Foreign researchers have demonstrated that the interaction between malignant cells and immune components can have a dual biological effect: an effective immune response may inhibit tumor development, whereas the establishment of immune tolerance and an immunosuppressive microenvironment may promote tumor survival, invasion, and metastatic spread [3,4,7,11,12]. A considerable body of research has focused on the tumor microenvironment in thyroid cancer. Tumor-infiltrating lymphocytes, macrophages, dendritic cells, natural killer cells, stromal elements, and soluble mediators collectively form a complex regulatory network. Depending on their functional state and quantitative relationships, these components may either support an effective antitumor response or create conditions favorable for tumor progression. These observations have stimulated interest in identifying immunological parameters that may

complement established clinicopathological prognostic criteria [11,2,5,9]. Cytokines occupy a central position in the regulation of interactions between tumor cells and the immune system. They participate in inflammation, cellular proliferation and differentiation, apoptosis, angiogenesis, and the recruitment and activation of immune cells. Changes in cytokine production may therefore reflect both systemic and local processes associated with malignant tumor development. In thyroid cancer, particular attention has been paid to pro-inflammatory mediators and their possible association with more aggressive biological behavior.

IL-6 is a multifunctional cytokine involved in inflammatory and immune reactions and in intracellular signaling mechanisms associated with cell survival and proliferation. Its increased production has been reported in various malignant neoplasms and has been considered a potential marker of inflammatory activity accompanying tumor progression. In thyroid cancer, increased IL-6 concentrations may reflect activation of tumor-associated inflammatory mechanisms and changes in the interaction between malignant and immune cells. TNF-α is another key pro-inflammatory cytokine with complex and sometimes opposing effects in cancer biology. Depending on its concentration, duration of exposure, and characteristics of the tumor microenvironment, TNF-α may participate in antitumor reactions while also supporting chronic inflammation and signaling pathways favorable to tumor progression. Accordingly, its serum concentration may provide additional information about the intensity of systemic inflammatory and immunological responses. Available studies also indicate that traditional clinical and morphological parameters are not always sufficient to predict the individual course of thyroid cancer. Even among patients with highly differentiated tumors, disease progression, relapse, and metastatic spread may occur unpredictably. This has led investigators to search for objective laboratory markers that can be repeatedly measured during treatment and follow-up [6,8,10,13,20].

Studies conducted by researchers in Uzbekistan and other countries of the region have likewise emphasized the importance of assessing immune reactivity and inflammatory mediators in patients with malignant neoplasms. However, the available material presented in this article does not contain sufficient bibliographic information to reliably name individual local authors. Therefore, their specific contributions should be described in the final manuscript after the complete reference list has been verified. An analysis of the available literature shows that most previous studies have examined immunological alterations either as components of thyroid cancer pathogenesis or as isolated laboratory abnormalities. The distinguishing feature of the present study is the assessment of IL-6 and TNF-α dynamics before and after treatment, with particular emphasis on the possibility of using persistent post-treatment elevation of these cytokines as additional markers of residual inflammatory activity, treatment effectiveness, and subsequent risk-oriented follow-up. This approach may contribute to the development of a more comprehensive system for monitoring patients with thyroid cancer.

RESEARCH METHODOLOGY

The study included 101 patients with thyroid cancer who received treatment and were under observation at the National Specialized Scientific and Practical Medical Center of Oncology and Radiology of the Ministry of Health of the Republic of Uzbekistan, the Tashkent City Oncological Dispensary, and the Regional Oncological Dispensary of the Ministry of Health of the Republic of Uzbekistan from 2019 to 2026. All patients underwent a comprehensive examination using basic clinical and diagnostic methods to establish the final diagnosis. *Patient inclusion criteria:* adults aged 18 years and older with morphologically confirmed TC. Immunological studies were conducted before and after radical therapy. The control group consisted of practically healthy individuals of similar age and gender. *Patient exclusion criteria:* HIV/AIDS; neoplasms of other localizations; exacerbations of autoimmune, allergic, and other infectious diseases, including viral hepatitis B and C; pregnancy. Enzyme-linked immunosorbent assay (ELISA) was used to conduct immunological studies. It is a highly specific.

Table 1. SERUM VALUES OF CYTOKINES IN PATIENTS WITH TC, M±m, pg/ml

Group Names	IL-6	TNF-alpha
TC patients before treatment	42.53 ± 5.15 *, **	17.95 ± 2.58 *
TC patients after treatment	13.59 ± 4.72 *	9.72 ± 1.31 *, **
Control group	5.22 ± 1.14	3.65 ± 0.72

Note: - significance of differences with the control group; - significance of differences between groups. Before treatment, the IL-6 concentration in TC patients was 42.53±5.15 pg/ml, which was statistically significantly higher than that in the control group (5.22±1.14 pg/ml, $p<0.05$). Consequently, the IL-6 concentration exceeded the control value by approximately 8.1 times. After treatment, the IL-6 level decreased to 13.59±4.72 pg/ml, corresponding to a decrease of 68.0% relative to the baseline level ($p<0.05$). Despite the pronounced positive

dynamics, the IL-6 concentration after treatment remained approximately 2.6 times higher than that in healthy individuals ($p<0.05$), indicating the persistence of a certain degree of inflammatory activity and immunological disorders. Similar changes were observed in the TNF-α level. Before the start of therapy, its concentration was 17.95±2.58 pg/ml, which was statistically significantly higher than that in the control group (3.65±0.72 pg/ml, $p<0.05$), by almost 4.9 times. After treatment, the TNF-α concentration decreased to 9.72±1.31 pg/ml, representing a reduction of 45.8% relative to the initial value ($p<0.05$). At the same time, the indicator remained approximately 2.7 times higher than that in the control group ($p<0.05$). It should be noted that the presence of statistically significant differences not only between the patients and the control group but also between the indicators before and after treatment confirms the effectiveness of the conducted therapy in reducing the systemic inflammatory response. However, complete normalization of the studied cytokines was not achieved, which may indicate ongoing immune activation even after completion of the main treatment.

The obtained results are consistent with modern concepts of the immunopathogenesis of thyroid cancer. It is known that tumor tissue actively interacts with innate and adaptive immune cells, forming a chronic inflammatory microenvironment that promotes tumor growth, angiogenesis, invasion, and the development of metastases. IL-6 is one of the main cytokines activating the JAK/STAT3 signaling pathway. Its hyperproduction stimulates tumor cell proliferation, suppresses apoptosis, enhances the synthesis of vascular endothelial growth factor (VEGF), and contributes to the formation of immune tolerance and the development of drug resistance. High IL-6 concentrations are also associated with a more aggressive disease course, the presence of regional metastases, and an increased risk of relapse [11,17]. TNF-α plays a dual role in carcinogenesis. Despite its ability to induce the death of individual tumor cells, during chronic production, this cytokine helps maintain inflammation, extracellular matrix remodeling, NF-κB activation, and enhancement of the invasive potential of the tumor. An elevated TNF-α level is considered one of the indicators of tumor process activity and a poor prognosis [18,20,22,23]. The obtained data are in good agreement with the results of international studies in recent years. According to published studies, the IL-6 concentration in patients with differentiated thyroid cancer usually exceeds the values observed in healthy individuals by 3–10 times, with the maximum values observed in patients with advanced disease stages and the presence of metastases. After surgical treatment and combination therapy, most authors note a decrease in the IL-6 level by 40–70%; however, even several months after treatment, its concentration often remains above control values, reflecting the ongoing immune restructuring of the body.

Similar trends are described for TNF-α. In most foreign studies, its level in TC patients exceeds the values observed in healthy individuals by approximately 2–5 times, and after treatment, it decreases by approximately 30–60%, without reaching normal values. The results obtained in this study fit almost entirely within these ranges, confirming their high reproducibility and consistency with modern global data. It should be noted that the simultaneous determination of IL-6 and TNF-α allows for a much more objective assessment of systemic inflammatory process activity than the study of each marker separately. Their combined elevation reflects the severity of tumor-associated inflammation and can be used to monitor treatment effectiveness. The conducted study showed that patients with thyroid cancer experience pronounced activation of the systemic inflammatory response, accompanied by a significant increase in the concentrations of IL-6 and TNF-α in the blood serum.

CONCLUSIONS

Before treatment, the IL-6 level was elevated by 8.1 times and TNF-α by 4.9 times compared with healthy individuals ($p<0.05$). After the conducted treatment, the IL-6 concentration decreased by 68.0% and TNF-α by 45.8% ($p<0.05$); however, both indicators remained significantly higher than the control values: IL-6 by 2.6 times and TNF-α by 2.7 times. The obtained results indicate that therapy leads to a significant decrease in the severity of the inflammatory response but does not ensure complete restoration of immunological homeostasis. The persistent elevation of IL-6 and TNF-α after treatment can be considered a laboratory sign of residual inflammatory activity and a potential risk factor for disease progression. Thus, the determination of serum concentrations of IL-6 and TNF-α is advisable as an additional immunological biomarker for assessing the activity of the tumor process, monitoring the effectiveness of therapy, predicting the course of the disease, and conducting subsequent dynamic observation of patients with thyroid cancer.

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TIBBIYOT
TA'LIMI & INNOVATSIYALARI

2026. № 9

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