Clinical study of tumor necrosis factor –alpha and interleukin- 10 in serum of patients with lymphoma

Estudio clínico del factor de necrosis tumoral alfa e interleucina -10 en suero de pacientes con linfoma

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Abstract

Background: Cytokines may have an important function in lymphoma, local manufacturing of those cytokines causes multiple systemic effect in the peripheral blood

Aim: This study was performed to assess the role of tumor necrosis factor alpha and interleukin-10 in lymphoma patients.

Materials and Methods: This case-control study included (88) Participants were assembled at the Ibn Sina Teaching Hospital in Mosul and separated into two groups (58) patients with lymphoma and (30) healthy person. Specialized doctors were diagnosed the patients based on immunophenotyping and morphology using either immunohistochemistry or flow cytometry. The study included estimation of tumor necrosis factor alpha (TNF-α), interleukin-10(IL-10), C-reactive protein (CRP), platelets (PLT) and white blood cells (WBC), in patients with lymphoma compared to healthy group. The study also included estimating of these parameters after three months of chemotherapy.

Findings: The results clarified a significant rise at p≤ 0.05 in the levels of TNF-α (1170±73.5 vs 165.7 ±34.6), IL-10 (2266± 265.2 vs 92. 6 ± 6.38), CRP (88.4 ±4.2 vs 9.2±2.1), WBC (51.77±12.76vs 6.31±1.55) and a significant decrease in PLT (330±30.5 vs 100.09±24.67) in lymphoma patient in comparison to healthy. The results also showed a positive correlation between TNF-α with IL-10,CRP and WBC ,while there was a negative correlation with PLT (at p≤ 0.05). Also, the results clarified that levels of TNF-α and IL-10 were decreased significantly (at p≤0.05) to (886±63.8) and (988± 95.8) respectively after three months of chemotherapy.

Conclusion: The assessed levels of TNF- and IL-10 in lymphoma patients may play a significant role in lymphoma development and may be crucial for lymphoma diagnosis and treatment.

Keywords*:* Lymphoma, Tumor necrosis Factor alpha, Interleukin-10, Chemotherapy.

Antecedentes: las citocinas pueden tener una función importante en el linfoma, la fabricación local de esas citocinas provoca múltiples efectos sistémicos en la sangre periférica.

Objetivo: Este estudio se realizó para evaluar el papel del factor de necrosis tumoral alfa y la interleucina-10 en pacientes con linfoma.

Resumen

Materiales y métodos: este estudio de casos y controles incluyó a (88) participantes reunidos en el Hospital Universitario Ibn Sina de Mosul y separados en dos grupos (58) pacientes con linfoma y (30) personas sanas. Médicos especializados diagnosticaron a los pacientes basándose en inmunofenotipado y morfología mediante inmunohistoquímica o citometría de flujo. El estudio incluyó la estimación del factor de necrosis tumoral alfa (TNF-α), interleucina-10 (IL-10), proteína C reactiva (PCR), plaquetas (PLT) y glóbulos blancos (WBC), en pacientes con linfoma en comparación con grupo sano. El estudio también incluyó la estimación de estos parámetros después de tres meses de quimioterapia.

Hallazgos: Los resultados aclararon un aumento significativo en p≤ 0,05 en los niveles de TNF-α (1170±73,5 vs 165,7±34,6), IL-10 (2266±265,2 vs 92,6±6,38), PCR (88,4 ±4,2 vs 9,2±2,1), WBC (51,77±12,76 vs 6,31±1,55) y una disminución significativa en PLT (330±30,5 vs 100,09±24,67) en pacientes con linfoma en comparación con sanos. Los resultados también mostraron una correlación positiva entre TNF-α con IL-10, PCR y WBC, mientras que hubo una correlación negativa con PLT (en p≤0,05). Además, los resultados aclararon que los niveles de TNF-α e IL-10 disminuyeron significativamente (en p≤0,05) a (886±63,8) y (988±95,8) respectivamente después de tres meses de quimioterapia.

Conclusión: Los niveles evaluados de TNF- e IL-10 en pacientes con linfoma pueden desempeñar un papel importante en el desarrollo del linfoma y pueden ser cruciales para el diagnóstico y tratamiento del linfoma.

Palabras clave: Linfoma, Factor de necrosis tumoral alfa, Interleucina-10, Quimioterapia.

Introduction

Lymphoma is a heterogeneous mix of B-cell, T-cell, and occasionally helper killer cell cancers that commonly start in the lymph nodes but can affect any organ in the body. Expanded lymph nodes, fever, immersion sweats, unintentional weight loss, itching, and a persistent feeling of exhaustion are some possible signs and symptoms. The enlarged lymph nodes don't hurt. Sweats are prevalent and not rare at night[1].

(TNFα) is a Cytokine manufactured normally via Monocytes and Macrophages It is discovered in synovial cells and macrophages in the tissues. TNF serves a crucial role in the organization of immune cells. It's capable of result in Apoptotic cellular demise, to implicate irritation, and to obstruct Tumorigenesis and viral replication. Disorder of regulation of TNFα production has been implicated in a ramification of human diseases, including the major cancers. Recombinant TNFα used as an immune stimulant below the INN tasonermin. TNF-α can be manufactured ectopically inside the placing of malignancy and parallels parathyroid hormone each in inflicting minor hypercalcemia and within the carcinoma with immoderate manufacturing is related[2-4].

A frame of evidence has indicated that TNF-α mediates severe crucial techniques of tumor improvement, regarding the activation of oncogenes, DNA degradation, and dissemination of a tumor. The TNF-α overexpression is intently related to tumor recurrence and advantageous lymph node metastasis in CRC patients[5] IL- 10 is a pleiotropic cytokine recognized for its mighty anti-inflammatory and immune repressive consequences Originally recognized as a made of T helper cells, It's is now known to be manufactured by way of diverse Myeloid- and lymphoid-derived immune cells taking part in each innate and adaptive immunity[6]. Our research aimed to evaluate the role of TNF and IL-10 in lymphoma patients as well as their relationship to specific biochemical variables.

Materials and methods

This case- control study was done during the period from July 2022 to January 2023. It involved thirty healthy participants and fifty-eight lymphoma patients who were diagnosed by specialized doctors at Ibn Sina Teaching Hospital in Mosul city. Their age ranged from 20-60 years for both sexes. In accordance with the Helsinki Declaration, samples were taken after receiving the patients informed written consent. Inclusion criteria include all lymphoma patients diagnosed by histopathological and hematopathological examination, while exclusion criteria include lymphoma patients with fever and infection.

Biochemical analysis :

1- Competitive enzyme-linked immunosorbent assay (ELISA) was used to estimate

TNFα and IL-10. Cat. Nos. E0082Hu and 20211104 respectively. . 2- CRP was calculated by BIOLABO (France) Cat. No. 318128 using a colorimetric method.

3- Automated devices (cell-DYN, Ruby Abbott diagnostic USA) were used to measure PLT and WBC[7].

Statistical Analysis:

Software called SPSS version 28.0 was used to examine the data. T-test was used to describe the deference between the biochemical parameters in the groups (patients and healthy) (at diagnosis and after three months of chemotherapy) at the property of $P \leq 0.05$[8].

Results

According to the findings, patients had significantly higher levels of TNF, IL-10, CRP, and WBC than the healthy group, whereas there was a significantly lower level of PLT as can be shown in table 1.

According to the findings, TNF- was positively correlated with IL-10, CRP, and WBC and negatively correlated with PLT, as shown in table 2.

The results also indicate that the levels of TNF-α and IL-10 were significantly higher in older patients than younger one and in male than female patients and in advanced stages of the disease than earlier stages as shown in table 3 the stages of the disease were determined according to CT scan and bone marrow study.

Table 1: Concentrations of TNF-α, IL-10 and some biochemical parameters in lymphoma patients compared to healthy.

Biochemical parameters 1Mean ±SD	TNFα (pg/ml)	IL-10 (ng/L)	CRP (mmol/l)	PLT(plt/µl)	WBC ×1000/mm3)
Healthy (n=30)	165.7±34.6	92. 6±6.38	9.2±2.1	319±25.1	6.31±1.55
Patients (n=58)	1170±73.5*	2266±265.2*	88.4±4.2*	100.09±24.67*	51.77±12.76*

clarified a significant difference at $p \leq 0.05$

Table 2: Correlation between certain variables and TNF-a.

Biochemical parameters	Positive correlation	P value
IL-10	0.816	$p \leq 0.05$
CRP	0.308	$p \leq 0.05$
PLT	-0.278	$p \leq 0.05$
WBC	0.085	$p \leq 0.05$

Table 3: Correlation between TNF-α and IL-10 with the other parameters in lymphoma patients.

Parameter (Mean ± SD)		No.	IL -10	TNF-α	P value
Age (years)	<45	20	1940.89 ±90.5	886.89±70.5	$p \leq 0.05$
	≥ 45	38	2110.45 ±111.6	988.59±60.8	$p \leq 0.05$
Gender	Male	38	2320.76±160.5*	1386.29±110.5*	$p \leq 0.05$
	Female	20	1960.48±134.5	1040.79±120.6	$p \leq 0.05$
B- symptom	Positive	40	2200.98±184.9*	1218.89±90.5*	$p \leq 0.05$
	Negative	18	1999.89±174.5	1086.59±115.5	$p \leq 0.05$
Bulky disease	Positive	7	2400.56±164.6*	1311.29±95.85*	$p \leq 0.05$
	Negative	51	1950.76±194.6	1006.99±85.57	$p \leq 0.05$
Stage	Stage I	-			
	Stage II	8	1970.89±184.6	1045.59±118.5	$p \leq 0.05$
	Stage III	15	2220.78±157.7	1276.69±89.5	$p \leq 0.05$
	Stage IV	35	2500.26±166.6*	1486.59±105.5*	$p \leq 0.05$

indicate a significant difference at $p \leq 0.05$

The results clarified that TNF-α, IL-10 and WBC levels were reduced significantly after three months of chemotherapy while PLT concentration was significantly increased as shown in table 4.

Table 4 Effect of chemotherapy on TNF-α, IL-10 and biochemical parameters levels

Biochemical parameters	Groups (Mean ± SD)		P value
	patients before chemotherapy (at diagnosis)	patients after 3month of chemotherapy	
TNF-α (pg/mL)	1170± 73.5	886± 63.8*	p ≤ 0.05
IL -10 ng/L	2266± 265.2	988± 95.8*	p ≤ 0.05
WBC (×1000/mm3)	51.77±12.76	8.78±9.46*	p ≤ 0.05
Neutrophil %	1.59±0.50	6.70±1.25*	p ≤ 0.05
Plat (×1000/mm3)	100.09±24.67	200.48±29.88*	p ≤ 0.05

• indicate a significant difference at p ≤ 0.05

Discussion

The high concentrations of TNF-α and IL-10in serum of patients in our study was in agreement with pervious study which clarified that higher tumor burden and worse survival are correlated with high levels of these cytokines[9], or due to hemorrhagic necrosis in the body with suppressing of tumor vessel and ischemia. It additionally eases tumor cell lysis with the aid of activate anti-tumor immune reaction. TNF-α could work synergistically with different cytokines to activate tumor death[10]. TNF- has the ability to generate a variety of chemokines and cytokines, which can be employed as pro-tumorigenic sports activities with additional genetic change to tumor cells and activation of tumor cell duration[13], cytokines in malignant cells can stimulate nearby immunosuppression and angiogenesis[14]. The significant increase in of IL -10 levels in patients could be due to that Interleukins have validated to raise tumorigenesis by means of autocrine or paracrine mechanism and had a suppressive effect on the immune gadget directed against the tumor[15]. CRP is a delicate indicator to measure tissue injury. CRP levels are clearly elevated in cases of severe inflammation, and it can identify a variety of infections as well as damaged or necrotic cellular components by gathering with C-polysaccharide at the bacterial cellular wall. It uses a variety of compounds including C-polysaccharide and phospholipid in its administration, and it may activate the supplement device in the conventional approach to eliminate those infections and necrotic cells[16]. Our findings were comparable to Alwan AF et al study in that lymphoma patients' mean age was 52.43.1 years, with a range of 30-78 years[17]. In accordance with Yaqo RT. et al.'s findings, which reported a male predominance with a male to female ratio of 2:1, our data also revealed that the ratio of male to female lymphoma patients was 1.9:1[18]. The results also clarified that the higher percentage of the patients with stage IV and this can be explained by the lack of routine checkup which lead to late diagnosis in Iraqi patients, therefore they usually presented with advanced clinical stage. [19] In this study we found that there was positive correlation between TNFα, IL-10 level with stage of the disease, presence of B-symptoms, bulky disease and in male patients more than female patients which was in agreement with[20]. Patients with lymphoma saw a considerable decrease in TNF-, IL-10 levels during chemotherapy, and this decrease's magnitude was highly connected with the amount of therapeutic responses, raising the possibility that TNF-, IL-10 levels could serve as a predictor of chemotherapy response and prognosis[21]. TNF is linked to several recognized risk factors for lymphoma, including age, smoking, and obesity, so it may be a risk factor for those who have the disease[22]. These results suggest that TNF, IL-10 may play a role in tumorigenesis and may serve as a marker for cancer risk, therapeutic response, and prognosis in cancer patients.

Conclusions

The elevated levels of IL-10 and TNF found in lymphoma patients may be crucial in the growth of the disease. Their negative effects are associated with advanced disease stages, bulky disease, and B-symptoms.

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Study limitations:
Low sample size and conducting the study only in one city may prevent generalization of results.

Conflict of interest: None

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