Original Article

Possible Role of Interleukins 6 and 10 in Colorectal Carcinoma in Iraqi Patients

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Summary

Background : *It is quite accepted that interleukins (IL) in general play a crucial role in response to injuy , infection and on cogenic trans formation , among there are IL-6 and IL_10 .*

Aim of this study *is to find out the possible role of IL_ and IL – 10 in colo rectal carcima in Iraqi patients .*

Subjects and Methods: *forty patients with colorectal cancer (CRC) compased with 30 healthy controls were enrolled in this study. Serum conc. Of IL-6 and IL -10were estimated in both groups using ELIZA technique.*

Results: *Serem levels of IL-6 and IL-10 were significantly increased (P<0.001) in compassion with control group .*

Conclusion: *these cytokins could be used as a markers for tumor progression .*

Introduction

It is generally accepted that interleukins in general, are a massenger molecules that transmit signals between various cells of the immune system and secreted mostly by different subsets of lymphocytes and mononuclear phagocytic system (MPS) in responsc to injury, infection, and oncogenic transformations (1). Among these interleukins that are reported to be increased in CRC are IL-6 and IL-10 (2).

The first one is a pleiotropic cytokine which has a major role in acute-phase response to inflammatory episodes, hence considered as pro-inflammatory molecules with a potent effect on B cells as well as in malignant transformation and progression. (3).

Moreover, poor prognosis of patients with CRC has consistently been associated with IL-6 while it's immunosuppressive and anti-inflammatory properties were illustrated graphically in malignant tumors of plasma cell, hence, Huang et al., hypothesized that it may play a crucial role in immune surveillance (4).

On the other hand, Grotowski and Piechota (5) denoted that IL-10 level have estimated to be 13 times more in patients of CRC than control group and thereby considered as a marker for CRC.

In this study, levels of IL-6 and IL-10 were detected in patients with different stages of CRC compared with healthy control group

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Subjects and Methods:

Subjects:

Patients group: The current study comprised of 40 patients with primary CRC (18 females and 22 males; mean age 51.4 years, ranged between 24-75). They were among patients attending the gastroenterology and hepatology teaching hospital and Baghdad teaching hospital during the period between June till December 2002.

Tumors of CRC were staged by pathologist according to Dukes classification as seen in Table-1. Healthy control group: Was consisted of 30 apparently healthy individuals who have no history or clinical evidence of malignant disease. They were selected as normal control from blood bank donors, Their age and sex matched with patients group.

Estimation of IL-6 and IL-10:

These were determined in serum using commercially available ELISA and performed as recommended in leaflet with kit. (Immunotech, Beckman Coulter, France).

Statistical analysis: It was assessed using T- test and Kruskall-Wallis test.

Table-1 Stage classification (Dukes A-B) of the primary tumor.

Stage	Number
Dukes A	5
Dukes B	20
Dukes C	9

Dukes D	6

Results:

Primary tumors of 40 patients were localized according to Table-2, where 10 patients had the tumors in cecum and ascending colon, 13 in the descending and sigmoid colon and 17 in the rectum. Significant elevation of serum IL-6 level among patients with CRC (14.3pg/ml) compared with healthy control group (P<0.001) is clearly seen in Table-3. Moreover, highest serum concentration of IL-6 was recorded in stages C and D (36.3 & 109.0) compared to that in patients with stage A and B (6.9 & 11.4), as shown in Table-4 and Fig-1.

Concerning serum IL-10, obvious increase in CRC patients group (9.5pg/ml) compared with that of healthy control (5.2pg/ml) with P value <0.001 was clearly shown in Table-5, moreover highest concentration of this cytokine was clearly noticed in patients with advanced C and D (8.9 & 11.8pg/ml) in comparison with stages A and B (5.5 & 7.4pg/ml) respectively as clearly shown in Table-6 and Fig-2.

Table-2 Localization of the tumor

	NO.	Female	Male
Cecum ascending colon	10	4	6
Transverse colon	0	0	0
Descending sigmoid colon	13	7	8
Rectum	17	7	10

Table-3 The differences in median serum IL-6 concentration (pg/ml) between CRC patients and controls

	Study groups		
Values	CRC	H.C	P(T-test)
Minimum	3.1	2.0	
Maximum	160	9.9	
Median	14.3	5.9	P<0.001
N	40	30	

Table-4 The median serum IL-6 concentration (pg/ml) by stage of CRC

	Duke's staging system of CRC				
Values	A	B	C	D	P(Kruskall -Wallis)
Minimum	3.1	6.5	12.6	14.3	
Maximum	13.8	60.8	85.5	160.3	
Median	6.9	11.4	36.3	109.0	P<0.001
N	5	20	9	6	

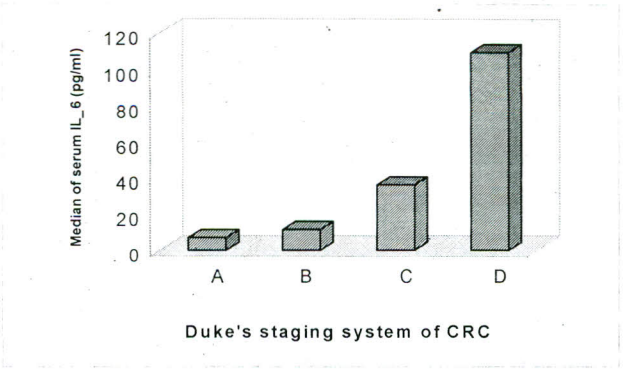

Figure-1: The median serum IL-6 concentration (pg/ml) by Duke's staging system of CRC.

Table-5 The differences in median serum IL-10 concentration(pg/ml) between patients and controls.

	Study groups		
Values	CRC	HC	P(T-test)
Minimum	1.9	0.9	
Maximum	15.6	8.0	
Median	9.5	5.2	P<0.001
N	40	30	

Table-6 The median serum IL-10 concentration (pg/ml) by stages of CRC.

	Duke's staging system of CRC				
Values	A	B	C	D	P (Kruskall-Wallis)
Minimum	1.9	3.0	4.1	4.0	
Maximum	8.3	10	12.2	15.6	
Median	5.5	7.4	8.9	11.8	P<0.001
N	5	20	9	6	

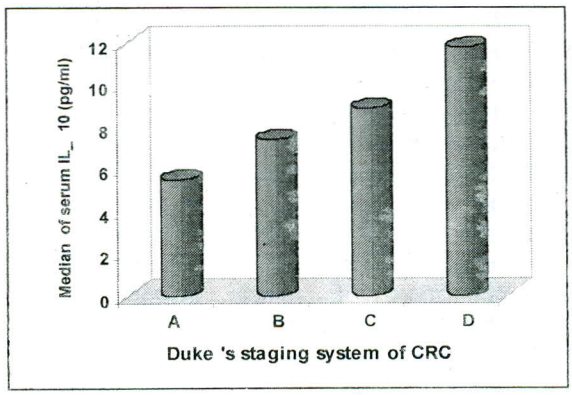

Figure-2: The median serum IL-10 concentration (pg/ml) by Duke's staging system of CRC.

Discussion:

In the last decades, focus was interestingly directed to the significant role of interleukins in progressing many oncogenic cells including CRC, since these cells are in general have taken the advantage of regulatory role of interleukins and thereby down regulating the appropriate immune responses targeted to destroy oncogenic cells (6,7,8).

In this study, high level of IL-6 in CRC was comparable with other studies (3,9) who reported similar increase of this cytokines; while Bataille (10) interestingly pointed out that high serum IL-6 concentration was reflecting the high tumor tissue concentration of this interleukin which indicated the proliferative activity of the tumor.

The serum elevation may quite well be due to the production of this cytokines by infiltrating immune cells (11) or by cancerous cells (12).

In a rather similar also, IL-10 play a crucial role in cancer progression and prognosis since IL-10 levels were significantly increased in CRC patients compared with control group, furthermore, this serum high level was clearly observed in advanced stages (C & D) than in patients with stages (A & B) These results consistent with many other studies (5,9,13) who denoted that IL-10 level correlated positively with extent, stages and tumor burden (14). The pronounced increase of serum IL-10 concentration could be due to the production of this cytokin by colon cancerous cells as reported by Gastle et al., (15).

Shortly these interleukins (IL-6 and IL-10) could be used as a markers for tumor progression and prognosis.

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