Original Article

Preoperative and Postoperative Serum Immunoglobulins Levels in Colorectal Cancer of Iraqi Patients

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Summary:

Background: *Quantitation of serum immunoglobulins (IgG, IgA and IgM) provides useful information for the evaluation of certain* ***cancers.***
Objectives:to *estimate serum immunoglobulins level before and after surgery, and to shed light on the correlation of immunoglobulins with progression of CRC.*
Patients and Methodes. *By single radial immune diffusion method IgG, IgA, IgM were estimated in 100 CRC patients preoperatively, and in 20 patients postoperatively compared with 35 patients control with ulcerative colitis (UC) and 50 healthy control.*
Results: *The study showed significantly increased the serum IgM level in patients group preoperatively ($p<0.001$) compared with control group. On the other hand, no significant differences were observed in respect to the mean of IgG, IgA, and IgM after surgical excision of the tumor in 20 patients.*
Conclusion: *These finding suggests that high level of IgM might be considered as prognostic indicator.*

Introduction:

The importance of humoral factors in immunological response to malignancy has been suggested by various investigators (l,2(_'1_3). The most consistently reported abnormality was found in studies of serum immunoglobulins, as well as circulating immune complex (CIC). Serological analysis showed a high level of IgG, IgA and IgM in CRC (4). Moreover, an increase of CIC levels in CRC patients compared to normal control was quietly reported (5&6).

As observed in many studies, auto-reactive antibodies against tumor associated antigen present in sera of patients with CRC is significantly higher, which is most likely due to polyclonal and specific activation of B-cells (7&8). Houbiers and associates mentioned that autoantibodies against " self " structure may provide additional information with regard to classification, treatment and prognosis of cancer patients (9).

Patients and Methods:

Patients:

The present study included 100 Arab, Iraqi CRC patients (42 females and 58 males; mean age 51.4 years, ranged between 21-81).

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Duke's classification and degree of differentiation are presented in Table-1, compared with 35 patients control (UC) and 50 healthy age and sex were matched control group.

Estimation of serum immunoglobulin:

Quantitative estimation of serum immunodiffusion immunoglobulin has been done by single radial.

Statistical Analysis:

It was assessed using ANOVA test and paired (T-test)

Table-1: Degree of differentiation and stage classification (Duke's A-D) of the tumor.

	Well Differentiated N=8	Moderately Differentiated N=74	Poorly Differentiated N=18
Duke's A	2	4	0
Duke's B	3	43	8
Duke's C	1	15	3
Duke's D	2	12	7

Results:

Tumors of the colon and rectum of 100 patients were localized according to Table-2, where 25 patients had the tumors in ascending colon, 6 in the transverse colon, 32 in the descending and sigmoid colon and 37 in the rectum

Table-2:Localization of the CRC

Location	NO.	Female	Male
Cecum, ascending colon	25	11	14
Transverse colon	6	1	5
Descending colon, sigmoid colon	32	13	19
Rectum	37	16	21

Table (3) pointed out to a significant changes in the level of IgM in CRC patients sera in comparison with healthy subjects. The results revealed that patients with CRC have a higher value of mean serum IgM level (160.5 + 64.34 mg/dl) with significant differences (P<0.001) compared to that of healthy subject (127.9 ±38.26 mg/dl).

While the mean serum levels of IgG and IgA showed no significant differences between CRC patients (1190.7 + 390.83 and 250.2 ±78.5 mg/dl respectively) and healthy control (1165.4 ± 137.52 and 228.4 ± 76.64 mg/dl respectively).

This study observed no changes in the mean serum IgG, IgA and IgM levels preoperatively (1133.1 ± 268.19, 1967 ± 6006: 143.3 ± 62.66 mg/dl respectively) when compared to their levels postoperatively (1160.8 ±361.1; 205 ± 70.91; 144.4 ± 64.47 respectively) as clearly observed in table (4).

Table -3: The difference in mean baseline immunoglobines (IgG, IgA, IgM) among the three study groups.

Serum IgG	***Colorectal***	***Ulcerative colitis***	***Healthy***	**P**
Minimum	**cancer cases**	***control***	***control***	***(ANOVA)***
	150.2	**710.8**	**757.1**	
Maximum	**2362.6**	**1701.2**	**1392.6**	
Mean	**1190.7**	**1223.6**	**165.4**	**NS**
Median	**1183**	**1210.2**	**1182.5**	
SD	**390.83**	**270.13**	**137.52**	
SE	**39.08**	**46.36**	**19.45**	
NO	**100**	**35**	**50**	
Serum IgA Minimum	**95.3**	**90.5**	**36.5**	
Maximum	**400.1**	**371.2**	**390.9**	
Mean	**250.2**	**277.5**	**228.4**	**NS**
Median	**241.1**	**290.1**	**215.8**	
SD	**78.5**	**71.66**	**76.64**	
SE	**9.19**	**13.44**	**10.84**	
NO.	**100**	**35**	**50**	
Serum IgM Minimum	**38.8**	**50.5**	**43.2**	
Maximum	**350.5**	**306.9**	**212.4**	
Mean	**160.5**	**169.7**	**127.9**	**<0.001**
Median	**140.2**	**141.6**	**132.3**	
SD	**64.34**	**79.8**	**38.26**	
SE	**6.43**	**13.49**	**5.41**	
NO.	**100**	**35**	**50**	

P (Bonferroni t-test)
CRC X' Healthy control' <0.001'
CRC X UC =0.86[NS]

Table-4: The mean change in serum immunoglobulines (IgG, IgA, and IgM) after surgical excision of the tumor in 20 patients with CRC.

	Baseline	Postoperative	Change	P(paired t-test)
Serum IgG	**549**	**327**	**-291.3**	
Minimum				
Maximum	**1791.3**	**1899.4**	**914.1**	
Mean	**1133.1**	**1160.8**	**27.7**	**NS**
Median	**1136.5**	**1130.9**	**-3**	
SD	**268.19**	**361.13**	**254.48**	
SE	**59.97**	**80.75**	**56.9**	
NO.	**20**	**20**	**20**	
Serum IgA	**91.3**	**95.7**	**-100**	
Minimum	**333.1**	**350.3**	**191**	
Maximum				
Mean	**196.7**	**205**	**8.3**	**NS**
Median	**214.3**	**212,2**	**-0.1**	
SD	**60.06**	**70.91**	**71.46**	
S E	**13.43**	**15.86**	**15.98**	
NO.	**20**	**20**	**20**	
Serum IgM	**43.2**	**42.1**	**-27.9**	
Minimum				
Maximum	**350.5'**	**350.5-**	**92.7**	
Mean	**143.3**	**144.4**	**1.1**	**NS**
Median	**132.3**	**129.6**	**-2.1**	
SD	**62.66**	**64.47**	**25.99**	
SE	**14.01**	**14.42'**	**5.81**	
NO.	**20**	**20**	**20**	

Discussion:

Quantitation of serum Igs (IgG, IgA and IgM) provides useful information for the evaluation of certain disease states. In CRC patients Igs levels have been investigated by various workers but their results were contradictory. The results of this work is in agreement with many investigators (1 &2) who collectively cited that serum levels of IgG and IgA in CRC patients were quite close to their concentrations in healthy control group (8).

While others reported that the mean of serum IgM was elevated in CRC in comparison to healthy control (4, 8 &10).

Furthermore, Slater and associates found an association between advanced stage of disease and a combination of low levels of IgA or high levels of IgM, as well as the ratio of IgA/IgM was also found to be lower in advanced disease. This was denoted that low levels of IgA and high IgM may represent an altered immune response and thus be a prognostic indicator (1).

The increased IgM levels in a significant proportion of CRC patients in the present study and the other concordant studies can be attributed to an increased antigenic stimulation suggesting a humoral defensive reaction against increasing tumor load.

Moreover, Hirano et al., showed that elevated IL-6 production by tumor cells was implicated in the hypergammaglobulinemia in cancer patients (I1).

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