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RESEARCH ARTICLE
ROLE OF IL10,TNF IN IRAQI PATIENTS WITH COLON CANCER

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ABSTRACT

Colorectal cancer (CRC) is the third most commonly diagnosed cancer among males and the fourth most common among females worldwide. investigated the serum levels of IL-10 and TNF-α in patients with colon cancer. Fifty patients with colon cancer (21 female and 29 male) with ages ranged between (20-70) years were taken from (Al-Hussain Hospital City/Kerbala, Digestive and Liver Disease /Education Hospital Medical City Baghdad and Teaching Oncology Hospital /Baghdad Medical City/ Baghdad /Iraq).Control group consisted of 20 healthy people who were free from signs and symptoms of cancer who matched in age and gender with patients, and had no history for any gastrointestinal problem.TNF-α(TNF-α-EASIA Kit, DIAsource) and IL-10 (IL-10-EASIA Kit, DIAsource) were studied using the enzyme-linked immunosorbent assay (ELISA) method.t-test and ANOVA and Pearson correlation used to analyze results by using SPSS version 19. P-value ≤ 0.05 was considered significant.Serum CEA,Ca19-9 ,IL10 and TNF- α were increased significantly ($p< 0.05$) in patients compared with control group,these parameters increased no significantly ($p>0.05$) after chemotherapy except IL-10,so increasing of CEA,Ca19-9,IL-10,and TNFα values at stage3(10.3±3),stage1 (52±9.5),stage4(49±23)stage1(148±16) respectively no significant($p>0.05$) among stages, the results revealed a strong correlation ($p<0.05$) between TNF and CA19.While there is no significantly correlation ($p<0.05$) found in the studying parameters in patients who did not treatment with chemotherapy drug. Significantly correlation of CEA,Ca19-9 ,IL10 and TNF- α with colon cancer, so increased no significantly ($p>0.05$) after chemotherapy except IL-10.

INTRODUCTION

Colorectal cancer (CRC) is one of the most common cancers that cause death in the Western world (Ries,*et al*,2007),so is the third most commonly diagnosed cancer among males and the fourth most common among females worldwide.CRC is a major cause of morbidity and mortality in Western developed countries, their age standardized rates are the highest in the world. The latter rates are much lower in developing countries in Asia and Africa. In Iraq, a developing Asian country in Eastern Mediterranean region, these rates are about fourfolds less than those in developed countries inEurope and North America(Parkin*et al*,2005).

However, CRC is the seventh most common cancer among Iraqis(Al-Hasnawi*et al* 2009).

IL-10 was described in 1989 as a cytokine produced by Th2 Th cell clones which inhibits macrophage APC-dependent cytokine synthesis by ThlTh cells(Fiorentino. and Mosmann,1989; Moore et al ,1990).IL-10 inhibits the ability of macrophage to stimulate cytokine synthesis by Thl Tcell clones(Fiorentino*et al*,1991a).IL-10 is an important immunoregulatory cytokine produced by many cell populations. Its main biological function is limitation and termination of inflammatory responses and the regulation of differentiation and proliferation of several immune cells such as T cells, B cells, naturalkiller cells, antigen-presenting cells, mast cells, and granulocytes(Asadullah*et al*,2003).

Carcinoembryonic antigen (CEA) was described in 1965 by Gold and Freedman (Gold and Freedman,1965a;Gold and Freedman,1965b),

when they identified an antigen that was present in both fetal colon and colon adenocarcinoma but to be absent from healthy adult colon, it was given the name carcinoembryonic antigen, or CEA,Because the protein was detected in only cancer and embryonic tissue, was also present in certain healthy tissues, its concentrations in tumors were on average 60-fold higher than in the nonmalignant tissues(Boucher *et al*,1989).

Serum CEA can be used as the chemotherapy on colorectal cancer(Shahbaa ,2011).Evidence enumerate carbohydrate antigen (CA) demonstrated that tumor-associated antigens are clinically useful for the diagnosis, staging of human gastrointestinal cancers, particularly colorectal cancer. It is sensitive and specific markers of this disease. Currently, the gastrointestinal cancer-associated carbohydrate antigen 19-9 (CA19-9) is the most widely employed as tumor marker in cancer diagnosis(Zhang*et al*,2013).

The aim of this study to estimate the serum level CEA,Ca19-9,IL10,TNFα in colon cancer patients.

Patients and Methods

Selection of patients

During the period 1/October/2013 to 1/March/2014, fifty patients with colon cancer (21 female and 29 male) with ages

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ranged between (20-70) years were taken from (Al-Hussain Hospital City/Kerbala, Digestive and Liver Disease /Education Hospital Medical City Baghdad and Teaching Oncology Hospital /Baghdad Medical City/ Baghdad /Iraq).

Control group consisted of 20 healthy people who were free from signs and symptoms of cancer who matched in age and gender with patients, and had no history for any gastrointestinal problem.

Sample collection and assay procedure

Blood sample (5ml) was collected left at room temperature and then centrifuge for 15 min. at (3000 rpm). Serum was then separated and freezed until time of analysis. Estimation of CEA,Ca19-9Vidas(Biomerieux SA/France),IL10,and TNFα ELISA kit (Cusabio/China) in serum using commercially available and performed as recommended in leaflet with kit

Statistical Analysis

Results are expressed as mean ± standard error mean (SEM), student t-test and ANOVA and Pearson correlation used to analyze results by using SPSS version 19. P-value ≤ 0.05 was considered significant.

RESULTS

A total of 50 patients with colon cancer divided into two groups according to the age (20-40)yrs16(32%),and age (41-70)yrs 34(68%),were 21(42%) patients female. The distribution of the patients according to pathological evaluation was as follows:4 stages(Ⅰ, Ⅱ, Ⅲ, Ⅳ)were 2(4%),13(26%),31(62%),4(8%) respectively table1 .

Table 1 Identifying Informations of Patients with Colon Cancer

Variable		No.	Percentage (%)
Total number of patients		50	100
•	Age		
a)	(20-40)yrs	16	32
b)	(41-70)yrs	34	68
•	Gender		
a)	Female	21	42
b)	Male	29	58
•	Stage of tumor diagnosis		
Stage:			
Ⅰ		2	4
Ⅱ		13	26
Ⅲ		31	62
Ⅳ		4	8
•	Drug		
a)	Chemotherapy treatment	18	40
b)	Without treatment	32	60

Serum CEA,Ca19-9 ,IL10 and TNF- α were estimated in 50 patients (21 female,29 male) compared with 20 healthy subjects, these parameters were increased significantly ($p< 0.05$) in patients compared with control group as in (table 2).

Table 2 Values of TNF, IL10, CA19 and CEA in control and patients of colon cancer.

parameters	Group	No.	Mean ± SEM	p-value
TNF(pg/ml)	control	20	87.6±8	0.001
	patient	50	129.7±5	
IL10(pg/ml)	control	20	9±1	0.001
	patient	50	41±6	
CA19(U/ml)	control	20	5±0.4	0.001
	patient	50	23±5	
CEA(IU/ml)	control	20	0.8±0.01	0.04
	patient	50	8.3±1	

While table 3showed no significantly ($p>0.05$) decrease in the level of IL10 when compared between the patient who treatment with and without chemotherapy drug, the measured levels of TNF-α, Ca19-9 and CEA were no significantly increased in the same group demonstrated in (table 3).

Table 3 Comparison of serum tumor markers between chemotherapy and non-chemotherapy patients.

parameters	Group	No.	Mean ± SEM	p-value
TNF(pg/ml)	Chemotherapy	18	128±9	0.9
	Non-chemotherapy	32	130±6	
IL10(pg/ml)	Chemotherapy	18	47±13	0.5
	Non-chemotherapy	32	38±7	
CA19(U/ml)	Chemotherapy	18	13±4	0.1
	Non-chemotherapy	32	29±8	
CEA(IU/ml)	Chemotherapy	18	8.5±4	0.9
	Non-chemotherapy	32	8±2	

Table4 ,figure 1 were revealed that the increasing of CEA,Ca19-9,IL10,and TNFα values at stage3 (10.3±3) ,stage1 (52±9.5),stage4(49±23)stage1(148±16) respectively no significant($p>0.05$)among stages (figure 1).So the age groups (20-40)yrs,(41-70)yrs was shown in (figure2) with no significantly ($p>0.05$) changes between the studying parameters and age group.

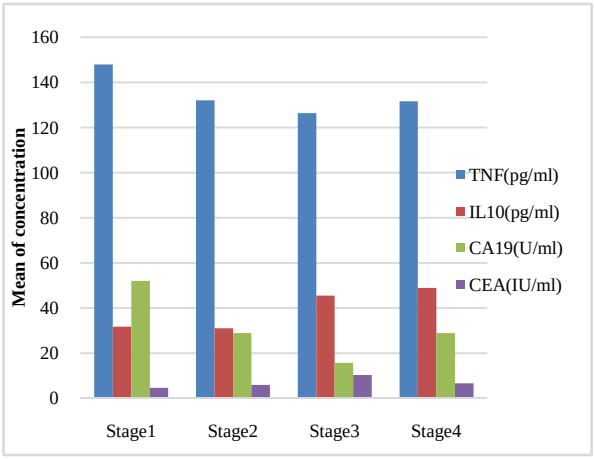

Figure1 revealed no significant ($p>0.05$) among stages and parameters.

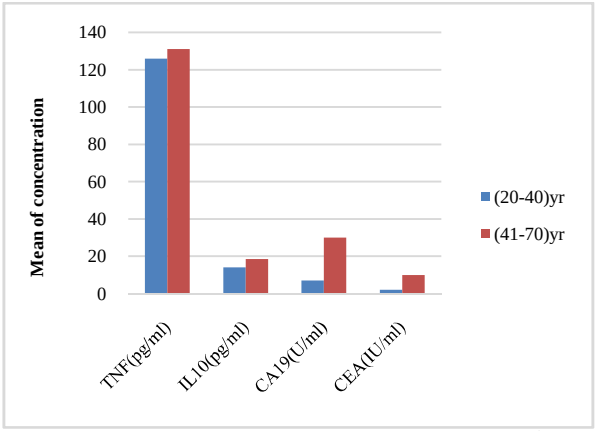

Figure 2 Age groups in TNF, IL10, CA19 and CEA no significant ($p>0.05$) between groups.

The correlation between the parameters in patients who treatment with chemotherapy drug was shown in (table 5) the results revealed a strong correlation ($p<0.05$) between TNF and CA19.While there is no significantly correlation ($p<0.05$) found in the studying parameters in patients who did not treatment with chemotherapy drug (table 6).

Table 4 Stage levels in TNF, IL10, CA19 and CEA no significant (p>0.05) between stages

parameters	Stage1 mean±SEM	Stage2 mean±SEM	Stage3 mean±SEM	Stage4 mean±SEM	P-value
CEA(IU/ml)	4.7 ± 1.5	6±2	10.3±3	6.6±4	p>0.05
CA19(U/ml)	52±9.5	29±9	15.8±6	29±13	
IL10(pg/ml)	31.8±22	31±10	45.6±10	49±23	
TNF(pg/ml)	148±16	132±7	126.4±8	131.6±10	

Table 5 Correlation between parameters in patient chemotherapy drug

parameters	r	p-value
TNF vs IL10	0.03	0.9
CA19 vs IL10	-0.04	0.08
CEA vs IL10	0.06	0.8
TNF vs CA19	0.6	0.01
TNF vs CEA	-0.06	0.8
CEA vs CA19	-0.07	0.8

Table 6 Correlation between parameters in patient not have chemotherapy drug

parameters	r	p-value
TNF vs IL10	0.03	0.8
CA19 vs IL10	0.3	0.09
CEA vs IL10	-0.2	0.3
TNF vs CA19	0.1	0.4
TNF vs CEA	-0.2	0.3
CEA vs CA19	0.2	0.2

DISCUSSION

Our results are agreement with studies on colorectal cancer patients that also demonstrated significant higher serum levels of CEA and Ca19-9 in comparison with the control group(Nada et al,2013),a lot of researchers believed that preoperative CEA level was associated with the tumor range (Yamashita and Watanabe,2009; Fiorentino*et al*,2010;Xu HX*et al* ,2011) might provide us important information to prediction the possibility of tumor peritoneal suffusion(Hyeon*et al*,2013).

Other study In the radiation only group, 21 (55 %) patients had raised CEA levels before the treatment, 18 (86%) of them decrease in CEA with CT response, 17(45%) patients with normal CEA. 15 (89%) of them showed normal CEA post treatment 12 (80%) of them showed CT response and 3 of them shows CT non-response. 2/17 (11%) patients showed further increase in CEA level(Sami *et al*,2012),so found that the level correlated highly with platelet count. They did not find any direct relationship with tumorexhaust. Most cytotoxic agents, and 5-FU,influence platelet counts. The mechanisms behind the decrease of Tissue Polypeptide –specific Antigen TPS and Vascular endothelial growth factor VEGF serum levels may thus be different (Berglan*et al*,2002).

Explain the significant increased level of serum IL-10 secretion is one of the mechanisms with which the tumor cells "avoid" the immunological oversight which at the end will also associate to raise the IL-10 serum level (Mocellin*et al*,2004), so observed Methylthioadenosine (MTA) can inhibit induced IL-10 expression in colon cancer in mice(Tony*et al*,2012).

Increase TNFα in colon cancer and decreased there levelsafter chemotherapy in our study agreement with anticancer drug for the treatment of colon cancer reduction in the level of TNF α(Ramesh *et al*,2013).

Mechanism of how TNF-α affects the development of cancer is unclear yet. It is speculated that it plays a role in the development of cancer via the production of DNA damage and the inhibition of the DNA repair mechanism. In addition to this, TNF may produce tumor invasion in colorectal cancer (Şeneland Kılıckap, 2010).

Explanation of this phenomenon may be TReg contribute in IL10 secretion in colon cancer as inflammatory response to eliminate tumor that induced cells like macrophages contribute in TNF secretions to promote apoptosis in tumor cells but chemotherapy decreased that.

CONCLUSION

Significantly correlation of CEA, Ca19-9, IL-10 and TNF- α with colon cancer, so increased no significantly (p>0.05) after chemotherapy except IL-10.

References

Al-Hasnawi SM, Al-Khuzaie A, AL-Mosawi AJ, Yonan OF, Fadhil HM, Sami S.2009. Cancer in Iraq: Distribution by primary tumor site. New Iraqi J Med;5:5-8.

Asadullah K, Sterry W, Volk HD.2003. Interleukin-10 therapy -- review of a new approach. *PharmacolRev* , 55**:**241-269.

Bergland,D.Molin,A.Larsson,R.Einarsson,&B.Glimelius.2002.Tumour markers as early predictors of response to chemotherapy in advanced colorectal carcinoma. Annals of Oncology, 13:1430 1437.

Boucher D, Cournoyer D, Stanners CP, Fuks A. 1989.Studies on the control of gene expression of the carcinoembryonic antigen family in human tissue. Cancer Res;49:847–52.

Fiorentino DF, Zlotnik A, Mosmann TR, Howard M, and O′GarraA.1991a.IL-10 inhibits cytokine production by activated macrophages. J Immunol 147**:**3815-3822.

Fiorentino F, Hunt I, Teoh K, *et al*.2010.Pulmonary metastasectomy in colorectal cancer: a systematic review and quantitative synthesis. J R Soc Med, **103**, 60-6.

Fiorentino. D. F., M. W. Bond. and T. R. Mosmann.1989.Two types of mouse helper T cell. 1V. Th2 clones secrete a factor that Inhibits cytokine production by Thl clones. ***J.*** Exp. Med. 170:2081.

Gold P, and Freedman SO. 1965.Demonstration of tumor-specific antigens in human colonic carcinomata by immunological tolerance and absorption techniques. J Exp Med; 121:439–62.

Gold P,and Freedman SO. 1965.Specific carcinoembryonic antigens of the human digestive system. J Exp Med;122: 467–81.

Hyeon Yu, Gyung-Mo Son, Yong-GeulJoh.2013.The clinical significance of preoperative serum levels of carbohydrate antigen 19-9 in colorectal cancer .J Korean Surg Soc.84:231 237.

Mocellin; F.M., Maricola and H.A., Young. 2004. Interleukin-10 and the immune response against cancer: a counterpoint. J LeukocBiol, 78: 1043-1051.

Moore. K. W.. P. Vieira, D. F. Fiorentino. M. L. Trounstine, T. A Khan, and T. R. Mosmann.1990.Homology of cytokine synthesis Inhibitory factor(1L-IO) to the Epstein Barr virus gene BCRFI. Science 248: 1230.

Nada A. Hassoa, Zainalabideen A. Abdullab. 2013.Evaluation of tumor biomarkers and cytokines in the detection and follow up of colorectal cancer. Ann Coll Med Mosul Vol. 39 No. 2.172 177.

Parkin DM, Bray F, Ferlay J, Pisani P .2005.Global cancer statistics ,2002, *CA* Cancer J. Clin.; 55:74–108.

Ramesh. K. Goyal1, RoshniP.Solanki.2013.Anticancer Activity of Acetone Extract of QuercusInfectoria Olivier Fagaceae in 1,2 Dimethyl Hydrazine Induced Colon Cancer. International Journal of Cancer Studies & Research, 2:102.

Ries,L.A.G., Melbert, D., Krapcho,M., Stinchcomb, D.G., Howlader,N., Horner,M.J., Mariotto,A., Miller,B.A., Feuer,E.J., Altekruse,S.F., Lewis, D.R., Clegg,L., Eisner,M.P., Reichman,M. and Edwards, B.K. (eds.) SEER .2007.Cancer Statistics Review, 1975–2005. National Cancer Institute, Bethesda, MD.

Sami Al-Asari, AlaaAbduljabbar, Nasser AL-Sanea, Samar AL-Homoud, LuaiAshari and Khalid Balaraj. 2012.The Relation Between Serum CEA Response and the CTscan Finding After Neoadjuvant Therapy in Rectal Cancer Patients,The Open Colorectal Cancer Journal, *5*, 14.

Şenel S, Kılıckap S. 2010.Anti-tumor necrosis factor therapy and cancer. Cumhuriyet Med J; 32: 132-6.

Shahbaa A. Al-Bayati. 2011.Assessment of serum carcinoembryonic antigen in colorectal cancer patients treated by surgery and chemotherapy. Irq J Pharm. Vol.11,No.2,:12-16.

Tony W.H.Li, Heping Yang, Hui Peng, Meng Xia, Jose´ M.Mato1 and Shelly C.Lu .2012.Effects of S-adenosylmethionine and methylthioadenosine on inflammation-induced colon cancer in mice. Carcinogenesis vol.33 no.2 pp.427–435.

Xu HX, Huang XE, Qian ZY, *et al*.2011.Clinical observation of Endostar® combined with chemotherapy in advanced colorectal cancer patients. Asian Pac J Cancer Prev, **12**, 3087 90.

Yamashita K, Watanabe M, 2009.Clinical significance of tumor markers and an emerging perspective on colorectal cancer. *Cancer Sci*, **100**, 195-9.

Zhang S, Chen Y, Zhu Z, Ding Y, Ren S, Zuo Y.2013.Differential expression of carbohydrate antigen 19-9 in human colorectal cancer: A comparison with colon and rectal cancers.MolClinOncol. Nov;1(6):1072-1078.

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