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Interleukin (IL) 17 expression in Iraqi bladder carcinoma Patients

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Abstract: Interleukin (IL- 17) is pro inflammatory cytokines produced by CD4+ T-helper17 (Th17)cell .It has a vital effect on cells of the immune system playing crucial roles in pathogenesis of immune-mediated diseases, like-cancers. The current study was designed to detect the protein expression of IL-17 in Iraqi bladder carcinoma patients, and its correlation with clinical grades. Tissue samples were collected from 45 patients with bladder carcinoma. The immunoexpression of IL-17 was detected by using IL-17 monoclonal antibody. The results of Immunohistochemical (IHC) studying showed that tissues with positive (IL-17) expression were low in bladder cancer patients practically in low grades with significant difference, it is concluded that IL-17 expression can be used as indicators for procession in bladder cancer.

Key word: IL-17, Bladder Cancer, IHC, Carcinoma .

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Introduction:

IL-17 is a pro inflammatory intercessor on numerous cell types (1). There are various studies in IL-17 in raising inflammatory responses, information on the role of this interleukin in tumor evolvement are conflicting (2).

IL-17-secreting Th17 promotes inflammation and thus may promote both tumor growth and tumor regression. IL-17 appears to have protumor role in inflammation-associated cancer that relies on its proangiogenic property of surrounding endothelial cells and fibroblasts (3) Radosavljevic *et al*. disclosed IL-17 can work as a prognostic biomarker for colorectal cancer growth(4) . Wang *et al*. indicated it has a role in proliferation of cervical cancer cells by IL-6 (5). On the other hand, antitumor functions of IL-17 have also been famed. For example, IL-17 has been shown to induce IL-6 and IL-12 to stimulate tumor-specific cytotoxic lymphocyte development (6). Moreover, Muranski *et al*. showed that the release of IL-17 by Th17-polarized cells constituted tumors more effective than by Th1 cells (7) . Other study has revealed that IL-17 can provoke $CD8^+$ cytotoxic T lymphocyte responses by IL-2 and human leukocyte antigen I (HLA-I) against melanoma (8). IL-17 behaves as a port between the inflammatory response and cellular mediated immunity in cancer. IL-17 hastened expression of chemokines and matrix metalloproteinases enzymes in fibroblasts and lung epithelial cells, like to the actions of inflammatory cytokines TNF and IL-1 (9). Those data are uniform with many findings encouraging the idea of a proinflammatory role for IL-17 *in vitro* (10) .For the above data we aimed to

evaluate protein expression of the IL-17 in Iraqi patient with bladder carcinoma and to describe the relation between its expression and clinical grades.

Material & Method

Forty five biopsies tissues samples from patients with bladder carcinoma (BC) were included in this study, the patient samples were collected from AL-Yarmook Teaching Hospital. The diagnosis of these tissue blocks were based on the obtained histopathological records of bladder biopsy samples by pathologist in hospital laboratory. The tissue sections were put on positive charged slides and stained immunohistochemically for IL-17. Immunohistochemical staining was done using the Novocastra TM Polymer Detection Systems (Envision technique) by using commercial kit from Novocastra, Newcastle, UK, RE7150-K , the slides were de-waxed in xylene , rehydrated in graded alcohols then antigen retrieval carried out using microwave for ten minutes . All of the slides were treated with anti IL-17 monoclonal antibody, dilution 1:50 for overnight, then incubated with a post primary block solution for 30 minutes. In the next step the slides were rinsed gently in PBS 2× 5 and tissue sections incubated with a secondary antibody Novolink TM polymer mouse and rabbit immunoglobulins) for 30 minutes, washed in PBS 2× 5 . After washing, the samples were stained with diluted liquid DAB, and then counter stained with hematoxylin. Slides washed, dehydrated then mounting, and examining under light microscope at 10X,20X,40X magnification.

Results & Discussion

Most our study patients had transitional cell carcinoma as the type of bladder tumors Concerning the grading of the tumors , our study showed that most of patients presented with low grade G ≤ 1 tumor (53.3 %),while 46.7% were with high grade G ≥ 2 tumor (Figure 1) .

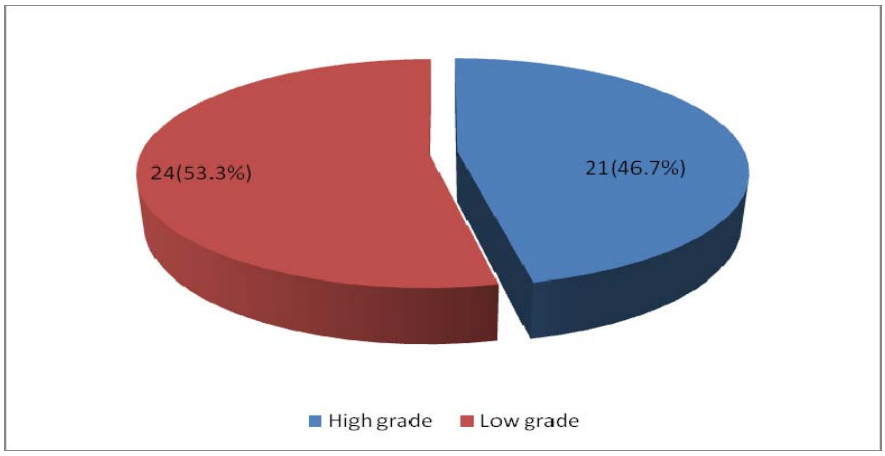
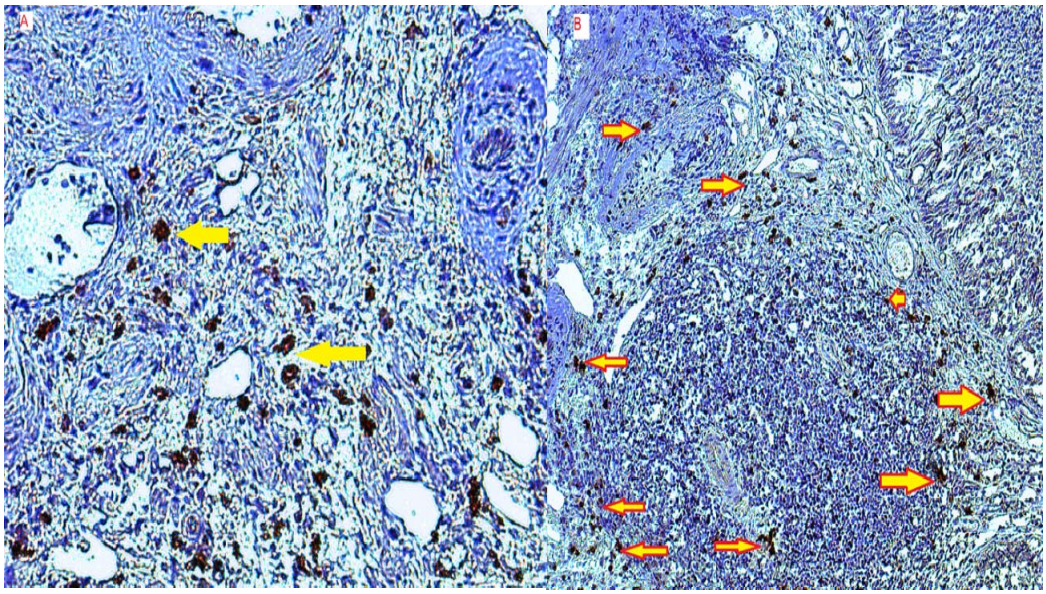


Figure (1): Pie chart showing the distribution of BC cases according to clinical grades

IL-17 is a multifunctional cytokine. It has dual effect on tumor development and antitumor immunity . In this study the patients with positive protein expression of IL-17 was low in comparison with those patients with negative expression (20 (44%), 25(56%),respectively) (Table 1). The majority of high grade tumor cases showed positive immunohistochemical IL-17 expression 13(65 %), while only 7 cases (35%) of low grade tumors showed positive immunohistochemical IL-17 expression, significant difference was noted (Table 1). Most of the patients that identified by positive anti-IL-17 reaction demonstrated moderate positive reaction (Figure 2). These results agreed with Baharlou *et al*. results in bladder cancer and breast cancer who found that patients are in low grade and early stage of cancer get significantly low levels of IL-17 (11,12) . These results possibly point sustainable chemotherapy and radiotherapy effects on oppress IL-17-procucing Th17 cells in early grades. Also, lower inflammation-induced IL-17 can be companion with absence of angiogenesis, while in tumor advancement, increased IL-17-producing Th17 is foressable (11). Thus, raised IL-17 in advance stage of cancer, and angiogenic factors agreed with the fact that IL-17 was evinced to induce metastasis through the expression of VEGF enhancing both angiogenesis and lymphangiogenesis, Afterwards, leading to metastasis of many tumors (13).

So, IL-17 cytokine can be used as an indicator for advancement and immune response to bladder cancer.



Figure(2): A: Immunohistochemical tissue expression of IL-17 in Bladder Cancer tissues showing moderate positive IL-17 immunostaining (Brown-arrow-20X). B: Positive IL-17 immunostaining (Brown-arrow-10X)

Table (1): The percentage of IL-17 expression in bladder carcinoma patients in relation to the tumor grade.

parameter		IL-17 EXPRESSION		Total	P-value χ2 –value
		positive	negative		
Grade of UBC	Low grade (G≤ 1)	7(35%)	17(68%)	24(53.3%)	0.0274 4.861 * *p≤0.5 significant
	High grade (G≥ 2)	13(65%)	8 (32%)	21(46.7%)	
Total		20	25	45	

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