Research Article,

Demographical Factors Estimation of Patients with Bladder Cancer in Basrah Province

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Abstract:
The aim of this study was to determine Immunomolecular expression of inflammatory interleukins (IL-4, IL-6 & IL-10) by using ELISA, conventional PCR and Sequencing technologies, to give acknowledge about the roles of these interleukins in patients with bladder cancer in Basrah province. A case-control study included 85 confirmed bladder cancer patients and 80 individual as a control group. Data about age, gender, smoking, alcohol drinking, family history, occupation, residency and clinical findings for all patients with urothelial carcinoma were collected. This study show the effect of demographical factors (age, gender smoking, family history, alcohol drinking, occupation and residency) in patients with bladder cancer. The study show significant effect of these factors with an increased the risk of bladder cancer.

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Introduction:
Urothelial carcinoma is a disease in which the lining of the bladder lose their ability to regulate their growth and begin to divide uncontrollably, this abnormal growth can form a tumor, This abnormality may be caused by secondary chronic inflammation of lower urinary tract, stones, smoking and exposure to various chemicals, exposure to carcinogens products and compounds, and secondary schistosomiasis (Cohen *et al.*, 2000). Bladder cancer is a heterogeneous either, low-grade, superficial papillary lesion or high-grade, invasive tumor that usually has metastasized at the time of presentation (Ferri, 2003). Transitional cell carcinoma accounts for almost 5% of all human cancers and represents 95% of all urothelial tumors (Ashoor, 2007). It is the second most common tumor of the genitourinary tract; it's also the second most common cause of death from these cancers (Williams *et al*., 2001). It is the most common malignant tumor in the Western countries and the fifth most common cancer among males with an incidence of 29.8 per 100.000 males per year (Ashoor, 2007).in addition, it is the most common malignant tumor in the Middle East and Africa where Schistosomiasis is a prevelant problem

(Kadhim, 2009). In Iraq it's the third most common malignant tumor with incidence 6.6% in both males and females reported by Iraqi cancer registry (ICR), It's the second most common tumor in males (10.3%) and the eighth in females (3%)(ICR, 2000). Along the lines of many malignancies the incidence of bladder cancer increase with age, 89% of bladder cancer patients within 55 years or older (Prout, *et al.,* 2005). The smoking considered as the most common risk factor for bladder carcinoma because the cigarette smoke contain a lot of chemicals which are reach to the blood through the lung and finally flittered by the kidney and stored inside the bladder and these chemicals are in long term contact with the transitional epithelium lining of the bladder. Furthermore the family history of bladder cancer is related to the risk of bladder cancer, but quantifying the additional risk in different populations is still a related issue. Many occupations involve exposure to a specific substances that may increase the risk of bladder carcinoma. Among occupational-related bladder cancer cases, workers exposed to aromatic amines have the highest incidence rate. In addition Aacohol consumption accounts about more than 5% of male and 1.7% of female with malignancies
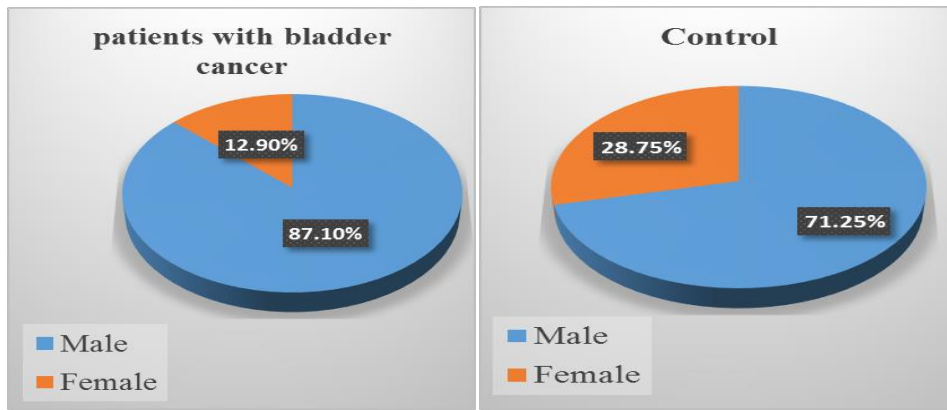
in the world (Boffetta, *et al.,* 2006).

Material and method:
A Case-control study was conducted between October 2020 to July 2021 which carried for patients with bladder carcinoma according to minimum sampling size equation that depend on the disease ratio, the total number of bladder cancer patients involved in this study are (85) individual were taken from Basrah oncology center in Basrah province, the age of patients range from 30->60 years and (80) individual considered as control group after they were checked and confirmed to be free from any urological or any other clinical problems. During collection process data about each patient were reported in questionnaire paper for each one, which included age, gender, family history, smoking, alcohol drinking, occupation, residency and clinical findings of the disease which we have highlight in the current study

Statistical analysis:
Statistical analysis was carried out by using SPSS VER.23 two way T test (student's T-test) and chi square to find out the statistical differences between all variables. Probability less than 0.05 is significant (P<0.05).

Results:
Table (1) Illustrate that the most age group of patients suffering with bladder cancer was (>60) were 51 (60.0%) from total study cases 85 (100.0%), at the fourth to fifth decades (40-49) (the number of bladder cancer was 9 (10.6%), while less cases of bladder cancer appeared at third to fourth decade (30-39) were 4 (4.7%) from total study cases. Statistically this differences was non-significant (P-value=0.2)

Table 1: Distribution of studied groups according to age group

Age group (Years)		Bladder cancer patients	Control	Total
(30-39)	NO.	4	0	4
	%	4.70%	0.00%	4.42%
(40-49)	NO.	9	24	33
	%	10.60%	30.00%	20.00%
(50-59)	NO.	21	24	45
	%	24.70%	30.00%	27.27%
(>60)	NO.	51	32	83
	%	60.00%	40.00%	50.30%
Total	NO.	85	80	165
	%	100.00%	100.00%	100.00%
Chi-square	3.82			
P-value	0.2 (N.S)			

Figure (1) observed that the most cases of bladder cancer recorded among male groups 74 (87.1%) versus 11 (12.9%) for female group from total study cases 85 (100.0%).Statistically this differences was non-significant (P-value=0.1)

Figure 1: Distribution of studied groups according to gender

Figure (2) observed that a more cases of bladder cancer recorded among patients that resident in peripheral area of Basrah 43 (72.88%) versus 42 (39.62%) in Bashra center from total study cases 85 (100.0%). Statistically this differences was non-significant (P-value=0.06)
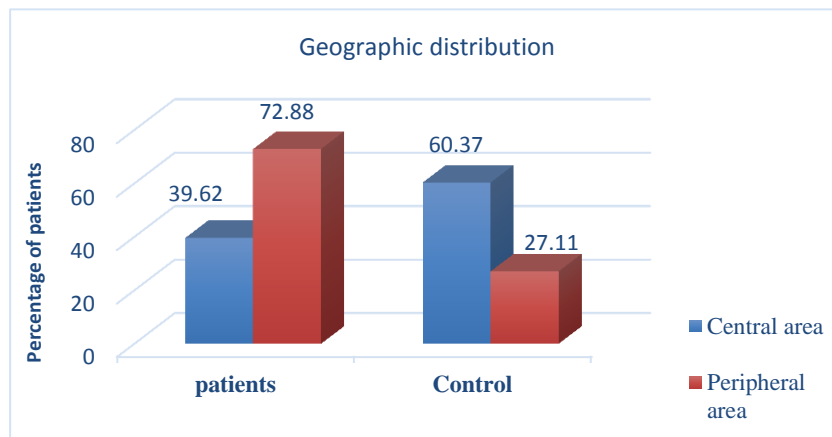

Table (2) document that most cases of bladder cancer patients within the age group (>60) were 26 (61.9%) are from Basrah-center and 25 (58.1%) are for Basrah-peripheral, at the fourth to fifth decade (40-49) most cases which were 7 (16.3%) for Basrah-peripheral and less cases 2 (4.8%) are for Basrah-center, while at third to fourth decade (30-39) most cases 3 (7.0%) for Basrah-peripheral and 1 (2.4%) for Basrah-center. Statistically this differences was non-significant (P-value=0.1)

Table (2) Residency of studied patients among various age groups

Age group (Yrs)		Residency status		Total
		Basrah-center	Basrah-peripheral	
30-39	NO.	1	3	4
	%	2.40%	7.00%	4.70%
40-49	NO.	2	7	9
	%	4.80%	16.30%	10.60%
50-59	NO.	13	8	21
	%	31.00%	18.60%	24.70%
>60	NO.	26	25	51
	%	61.90%	58.10%	60.00%
Total	NO.	42	43	85
	%	100.00%	100.00%	100.00%

Chi-square	4.9
P-value	0.1 (N.S)

Table (3) observe that the number of cases of age group (>60) which attacked with bladder cancer and smoking (regardless various types of smoking) were 39 (56.5%) from total study cases 69 (100.0%) versus non-smoker cases under the same age group were12 (75.0%) from total study cases 16 (100.0%). Statistically the differences significant (P-value=0.05)

Table (3): Distribution of Bladder cancer patients according to age group (Years) with smoking status

Age group (Yrs)		Smoking status		Total
		Yes	No	
(30-39)	NO.	4	0	4
	%	5.80%	0.00%	4.70%
(40-49)	NO.	8	1	9
	%	11.60%	6.30%	10.60%
(50-59)	NO.	18	3	21
	%	26.10%	18.80%	24.70%
(>60)	NO.	39	12	51
	%	56.50%	75.00%	60.00%
Total	NO.	69	16	85
	%	100.00%	100.00%	100.00%
Chi-square	2.3			
P-value	0.05 (N.S)			

Figure (3) document that all smokers 69 (100%) were males, while most non-smoking cases 11 (68.8%) from the total 16 (100%) were female.
Statistically the differences was highly-significant (P-value=0.00)

Figure (3) Distribution of Bladder cancer patients according to gender with percentage of smoking status

Table (4) document that most alcohol drinking patient with bladder cancer were within the age group (>60) which are 13 (61.9%) from the total study cases 21 (100%) versus non-alcohol drinking under the same group were 38 (59.4%) from the total study cases 64 (100%) Statistically the differences was non-significant (P-value=0.7)

Table (4): Distribution of   Bladder cancer patients according to age groups with alcohol status

Age group (Years)		Alcohol drinking		Total
		Yes	No	
(30-39)	NO.	1	3	4
	%	4.80%	4.70%	4.70%
(40-49)	NO.	1	8	9
	%	4.80%	12.50%	10.60%
(50-59)	NO.	6	15	21
	%	28.60%	23.40%	24.70%
(>60)	NO.	13	38	51
	%	61.90%	59.40%	60.00%
Total	NO.	21	64	85
	%	100.00%	100.00%	100.00%
Chi-square		1.08		
P-value		0.7 (N.S)		

Figure (4) observe the relation between male and female with alcohol drinking, as we see all cases drink alcohol which 21 (100%) are males while 0 (0%) are female. Statistically the differences was significant (P-value=0.04)

Figure (4): Distribution of   Bladder cancer patients according to gender with alcohol status

Table (5) observed that occupational status in the age group (>60) which attacked with bladder cancer are work with different types of jobs 27 cases (73.0%), 7 (46.7%) military and 6 (66.7%) industrial workers under the same age group, while no cases of bladder cancer were founded in teaching place under the both age group (30-39) and (40-49) respectively. Statistically the differences was significant (P-value=0.04).

Table (5): Distribution of Bladder cancer patients according to age group (Years) with occupation

Age group (Years)		Occupation status					Total
		Industrial	Teaching	Military	Without work	Others	
(30-39)	NO.	1	0	2	1	0	4
	%	11.10%	0.00%	13.30%	50.00%	0.00%	5.90%
(40-49)	NO.	0	0	3	0	3	6
	%	0.00%	0.00%	20.00%	0.00%	8.10%	8.80%
(50-59)	NO.	2	3	3	1	7	16
	%	22.20%	60.00%	20.00%	50.00%	18.90%	23.50%
(>60)	NO.	6	2	7	0	27	42
	%	66.70%	40.00%	46.70%	0.00%	73.00%	61.80%
Total	NO.	9	5	15	2	37	68
	%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%
Chi-square		21.28					
P-value		0.04 (S)					

Figure (3-6) documented that 11.7% of patients with bladder cancer are associated with family history while 88.23% without family history.
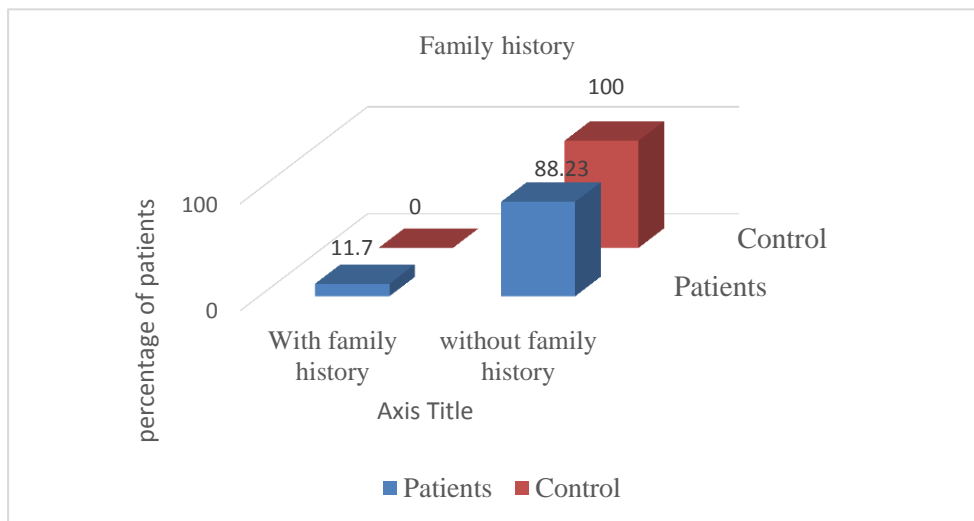
Figure (3-6): Association between bladder cancer and family history.

Discussion

In corresponding to gender the incidence rate of bladder cancer patients reveled high rate among males was 74 (87.1%) in comparison to females 11 (12.9%) from the total cases 85 (100%). This results is identical and conforming the data documented by other investigators (Ashoor, 2007; Hayder, 2004; Johansson & Cohen, 1997 and Zhang, 2014). This disparity could be explained due to exposure to environmental factors whereas few number of females work outside the house and reduced exposure to industrial carcinogens, physiological and anatomical body differences, sex hormones (androgens), and low tobacco intake among women's (Gupta *et al.,* 2009 and Ferlay *et al.,* 2013).

The present investigation demonstrated that the most important risk factors for bladder carcinoma were old age and smoking which agree with other studies (Cao *et al*., 2005; Brauers and Jakse, 2000 and Benson *et al*., 1983). Along the lines of many malignancies the incidence of bladder cancer increase with age, 89% of bladder cancer patients within 55 years or older at the onset of disease detection this estimated by Surveillance Epidemiology and End Results program (SEER), The National Cancer Institute (NCI) and (Prout, *et al.,* 2005). In our study most patients with bladder cancer concentrated within the age group (>60) years was 51 (60.0%) followed by the age group (50-59) years was 21 (24.7%), the third age group (40-49) years was 9 (10.6%), and finally the last age group (30-39) years were 4 (4.7%) which represent the lowest percentage and the incidence of the disease increased with age was nearly similar to (Helpap ,2002) and confirm the fact that indicate the association between smoking and the higher rates of comorbidities (Jha, 1999) other study indicate that age factor of the patients considered as a very risk factor because it's may contribute with the treatment decision of patients with bladder malignancy since most of them have other pathological conditions could influence the administration of surgical therapy (Prout, *et al.,* 2005). such an increase may be due to the genetic alterations that were frequently seen in older age group and were extremely rare in young group, of which such neoplasms appear to be of distinct biological type as well as, it usually noted in most cases that it lack genetic instability (Wild, *et al.,* 2007)

Regarding the smoking status which considered as the most common risk factor for bladder carcinoma, in this study 69 (81.17%) of cases are smokers and all of them are males while 16 (18.82%) are non-smokers from the total cases 85 (100%) . The result of this study is agreed and nearly identical with the study of (Abdul Ghafor, 1995; Cao *et al.,* 2005; and AL-khatib, 2007). Mostly long-term of intensive smoking was recorded to increase the possibility of bladder cancer occurrence (Brennan *et al.,*2000; Volanis *et al.,*2010 and Freedman *et al.,*2011) According to this investigator the number of age group cases (>60) which attacked with bladder cancer and smoking the cigarettes were 39 (56.5%) from total study cases 69 (100.0%) versus non-smoke cases under the same age group was 12 (75.0%) from total study cases 16 (100.0%).It was found that smokers have an overall risk level around 2-4 times from that of lifelong non smokers which proved by many epidemiological studies, whereas high risk of bladder cancer seems to be predominantly limited to smokers and increase with elevating the numbers and duration of smoking (Vineis ,*et al.,* 1984 and Castelao, *et al.,* 2001) . The cigarette contain a lot of chemicals which are reach to the blood through the lung and finally flittered by the kidney and stored inside the bladder and these chemicals are in long term contact with the transitional epithelium lining of the bladder, Metabolic enzymes are considered to be involved in either the detoxification or activation of chemical carcinogens on tobacco smoke, which have been suggested as possible genetic susceptibility factors for smoking-related malignancies (Sweeney, *et al.,* 2000 and Cao, *et al.,* 2005). In this study more cases of bladder cancer founded among patients resident in peripheral area of Basrah 43 (95.6%) versus 42 (84.0%) in Bashra center from total study cases 85 (100.0%). Statistically the differences was non-significant and cases distribution within the age groups found the patients within the age group (>60) was 26 (61.9%) are from Basrah-center and lowest was 25 (58.1%) are Basrah-peripheral, at the fourth to fifth decades (40-49) most cases which were 7 (16.3%) Basrah-peripheral and less cases 2 (4.8%) are Basrah-center, while at third to fourth decade (30-39) most cases 3 (7.0%) from Basrah-peripheral and 1 (2.4%) from Basrah-center, these results are agree with study done on Basrah population where it was found more cases (65%) in peripheral area of the city and less cases (35%) in the center of Basrah (Al-Shakour *et al.,* 2014).

The family history of bladder cancer is related to the risk of bladder cancer, but quantifying the additional risk in different populations is still a related issue. In addition, the role of family history of other cancers on bladder cancer risk remains unclear (Turati, *et al.,* 2017). In this study the data demonstrated that there are about 10 (11.7%) of patients had a family history with bladder cancer of first-relatives degree while 75 (88.23%) without history of bladder carcinoma, the result of this study match with recent study done in Baghdad province (AL-biaty, 2015) that found (12.2%) of the total cases had a history with UBC maybe because both studies conducted on the same population (Iraq), while doesn't agree with other study conducted in united states which

estimated that 33% of bladder cancer patients have cancer family history (Zhang, *et al.,* 2014). Among the hereditary factors involved in bladder cancer carcinogenesis, the role of variation in the genes coding for xenobiotic biotransforming enzymes such as N-acetyltransferase 2 (NAT2) and glutathione S-transferase M1 (GSTM1) has been most extensively studied (Murta-Nascimento, *et al.,* 2007) Alcohol consumption accounts about more than 5% of male and 1.7% of female with malignancies in the world (Boffetta, *et al.,* 2006). Moderate and heavy alcohol drinking did not significantly increase the risk of bladder carcinoma. However, heavy drinking may increase the risk of BC in males and certain groups of populations (Vartolomei, *et al.,* 2019).

This study as documented that most alcohol consumption patient were within the age group (>60) which were 13 (61.9%) from the total study cases 21 (100%) versus non-alcohol drinking under the same group were 38 (59.4%) from the total study cases 64 (100%) Statistically the differences was non-significant, this findings agree with study that confirm that there was no association with bladder cancer was observed (OR = 1.00, 95% CI 0.89–1.10) in either overall alcohol intake group (Mao, *et al.,* 2010). components of alcoholic beverages and their metabolites are excreted through the urinary tract, In particular, acetaldehyde, the primary breakdown product of ethanol in the body, has been shown to cause damage to the DNA, is classified as carcinogenic to humans and has been detected in the urine, On the other hand, alcoholic beverages have also a diuretic effect that may lead to higher frequency of voiding and thus decreased exposure of the bladder epithelium to carcinogens (Pelucchi, *et al.,* 2012). It was also found in the current study the relation between male and female with alcohol intake, all cases taken alcohol which were 21 (100%) were males while 0 (0%) were female, Statistically this differences was significant which correspond with other study that reported somewhat higher pooled estimate of relative risks (RRs) in men than in women (Pelucchi, *et al.,* 2012). The nature of Iraqi community and commitments with social traditions and ethics limits alcoholic consumption by women more than men /and this correlate with high incidence rate among men than women in Iraq. Many occupations involve exposure to a specific substances that may increase the risk of bladder carcinoma. Among occupational-related bladder cancer cases, workers exposed to aromatic amines have the highest incidence rate, and workers exposed to polycyclic aromatic hydrocarbons and heavy metals have the highest mortality rate (Pelucchi, *et al.,* 2006). In this study as shown in the table (3-5) we observed that the age group (>60) which attacked with bladder cancer their occupational status were work with different types of jobs 27 cases (73.0%), 7 (46.7%) military and 6 (66.7%) industrial workers under the same age group, while no cases of bladder cancer were founded in teaching place under the both age group (30-39) and (40-49) respectively. Statistically this differences was significant (P-value=0.04), this result correspond with another study which suggest that smoking military individual may portend a much higher cancer risk in this group (Thompson, et al., 1987) and confirm further study result which proposed that highest individual reported incidence risks were for factory workers (Cumberbatch, *et al.,* 2015).

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