Association of some interleukins in patients with surgical treatment of prostate cancer

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Abstract :

Aim of study : The aim of this study was to determine the interleukin levels in patients having prostate cancer surgery.**Patients and Methods:** The current data was collected for referred patients from March 2023 to October 2023 at the Iraqi Center of Cancer and Medical Genetics Research, Using sandwich ELISA kits, the levels of the cytokines IL-6 and IL-8 were assessed in serum of 25 healthy, normal controls and 50 prostate cancer patients undergoing treatment.Every participant in the study had to be at least 40 years old. Men with a PSA of less than 4 ng/ml and no history of prostate cancer served as controls. Male patients receiving androgen deprivation therapy had a histological diagnosis of prostate cancer.**Results :**the number of prostate cancer patients with surgical treatment was highest (P < 0.05) in the age group of 61≤ years (25 , 41.6%), followed by the age group of 51- 60 years (21 , 35 %) , So serum IL-6 was significantly higher (33.91 ±2.81 pg/ml) in patients without surgical treatment as compared to patients with surgical treatment (27.01±3.31) However,Serum IL-8 was significantly higher (203.9 ±□3.82 pg/ml) in patients without surgical treatment as compared to patients with surgical treatment (118.10 ±□4. 99)as well as in control group (71.872±31.22 pg/ml).**Conclusion:** Both IL-6 and IL-8 are important biomarkers in the context of prostate cancer. Their levels can provide insights into disease status and treatment response. Monitoring these cytokines may help in assessing the effectiveness of surgical interventions and in understanding the underlying inflammatory processes in prostate cancer patients.

Key words : PSA, prostate cancer, age specific PSA, reference range.

Introduction :

With the exception of non-melanoma skin cancer, prostate cancer (PC) is the second most prevalent cancer diagnosed and the fifth most common cause of cancer-related deaths in males globally (Zhou *etal.*,2016).In 2020, there were almost 1.4 million cases identified worldwide, with an age-standardized incidence rate (ASIR) of 30.7 per 100,000 males. While the age-standardized mortality rate (ASMR) is 8.3 per 100,000 in industrialized economies' continents with an ASIR of 59 per 100,000, it is 16.3 per 100,000 in African countries with low ASIRs of 30 per 100,000 (Wang *etal.*,2022) , Prostate cancer has been increasing in the Arab world despite having a low incidence there. Arabic men with PSA levels over 10 ng/ml are more common than Americans to have BPH, and Men from Europe with comparable levels were more likely to acquiring cancer of the prostate (Queem *etal.*,2013).

Proliferative inflammatory atrophy (PIA), a condition that results in chronic inflammation and regenerative risk factor lesions, is caused by a combination of infectious pathogens, genetic variation, dietary carcinogens, and hormonal imbalances(Marzo *etal.*,2007) , Androgen deprivation therapy is the cornerstone of treatment for prostate cancer, and it is frequently combined with other forms of treatment like chemotherapy, radiation therapy, and surgery [Cattrini *etal.*,2019].

According to the EAU guidelines on prostate cancer, some individuals with small T3, PSA <20 ng/ml, Gleason score <8, and a life expectancy >10 years may be candidates for radical prostatectomy in cases of locally advanced disease (Aus *etal.*,2001).

A number of growth factors, hormones, and cytokines are involved in the multi-step process that leads to the formation and progression of prostate cancer [Archer *etal.*,2020], so results of many studies showed the pro-inflammatory cytokines may play significant roles in encouraging the growth of tumor cells, and interleukins (ILs) may be exceptional markers of the aggressiveness and proliferation of prostate cancer cells (Wang *etal.*,2015 and Ugge *etal.*,2019).

Prostate cancer cell differentiation, apoptosis, proliferation, and resistance to treatment have all been demonstrated to be impacted by IL-6 [29]. The crossover point between high and low IL-6 levels was 16 pg/mL, according to one study that looked at IL-6 levels in patients with prostate cancer. It also found that high baseline IL-6 levels were linked to a poor response to chemotherapy (taxane) treatment [18]. While IL-8 is typically expressed at low levels in healthy conditions, tumour cells often exhibit heightened IL-8 secretion in response to stimuli, including external environmental factors or treatment-mediated stress, inflammation, and/or hypoxia [Korbecki*etal.*,2023].

Because of tumor extension outside the prostate and surgeons' limited capacity to remove a large margin of good tissue, surgical treatment is still debatable today. This is because drastic resection of the tumor may not be possible. Tumor recurrence and positive margins of resection result from this (van *etal.,1993*).

Surgical treatment of prostate cancer primarily involves the removal of the prostate gland and some surrounding tissue , The choice of surgical treatment depends on various factors, including the stage of cancer, overall health, and patient preference. It's important for patients to discuss their options thoroughly with their healthcare provider to determine the best approach for their specific situation.the main surgical options: Radical Prostatectomy: This procedure involves the complete removal of the prostate gland along with some nearby tissue, including the seminal vesicles and possibly nearby lymph nodes ; Transurethral Resection of the Prostate (TURP):Typically used for benign prostatic hyperplasia (BPH), this procedure can also be used in certain cases of prostate cancer to relieve urinary obstruction, but it does not remove the prostate entirely and Cryotherapy: This technique involves freezing the prostate tissue to kill cancer cells. It may be used for localized prostate cancer or in patients who have had recurrence after radiation therapy as well as High-Intensity Focused Ultrasound (HIFU): This is a minimally invasive technique that uses focused ultrasound waves to destroy cancer cells in the prostate.

Aim of study : The aim of this study was to determine the interleukin levels in patients having prostate cancer surgery.

Patients and Methods: The current data was collected for referred patients from March 2023 to October 2023 at the Iraqi Center of Cancer and Medical Genetics Research, Using sandwich ELISA kits, the levels of the cytokines IL-6 and IL-8 were assessed in serum of 25 healthy, normal controls and 50 prostate cancer patients undergoing treatment.Every participant in the study had to be at least 40 years old. Men with a PSA of less than 4 ng/ml and no history of prostate cancer served as controls. Male patients receiving androgen deprivation therapy had a histological diagnosis of prostate cancer.

Data analysis :

The software SPSS V. 24 (IBM USA) was used to analyze the collected data. For data analysis, the student t test with a P-value ≤ 0.05 was employed.

Results :

In table (1) showed the number of prostate cancer patients with surgical treatment (No.=60 , %) and without surgical treatment(No.=40 , %).

Table (1): Distribution of prostate cancer patients according to Age groups

Treatment status	Number of paetint	%
With Surgical Treatment	**60**	**60**
Without Surgical Treatment	**40**	**40**
Total	**100**	**100**

According to table (2), the number of prostate cancer patients with surgical treatment was highest (P < 0.05) in the age group of 61≤ years (25 , 41.6%), followed by the age group of 51- 60 years (21 , 35 %) and the age group of 40-50 years (14 ,23.3 %) as well as in prostate cancer patients without surgical treatment was highest (P < 0.05) in the age group of 61≤ years (16 ,40%), followed by the age group of 51- 60 years (14 ,35 %) and the age group of 40-50 years (10 ,25 %).

Table (2): Distribution of prostate cancer patients according to Age groups

Age groups (years)	Study groups		Control Study (Healthy)
	with surgical treatment	without surgical treatment	
	No. (%)		
40-50	14 (23.3)	10(25)	10(33.3)
51-60	21(35)_	14(35)	10(33.3)
61≤	25(41.6)	16(40)	10(33.3)
Total	60(100)	40(100)	30(100)

Table(3) and Figure(1) show serum IL-6 was significantly higher (33.91 ±2.81 pg/ml) in patients without surgical treatment as compared to patients with surgical treatment (27.01±3.31) as well as in control group (21.23± 2.92pg/ml). However,Serum IL-8 was significantly higher (203.9 ±□3.82 pg/ml) in patients without surgical treatment as compared to patients with surgical treatment (118.10 ±□4. 99)as well as in control group (71.872±31.22 pg/ml).

Table (3): comparing serum levels of interleukin-6 (IL-6) and interleukin-8 (IL-8) in prostate cancer patients with and without surgical treatment

Study groups	Levels of Interleukin	
	IL-6	IL-8
	Mean ± S.D	
with surgical treatment	27.01±3.31	118.10 ±□4. 99
without surgical treatment	33.91 ±2.81	203.9 ±□3.82
Control Study (Healthy)	21.23± 2.92	71.872±31.22

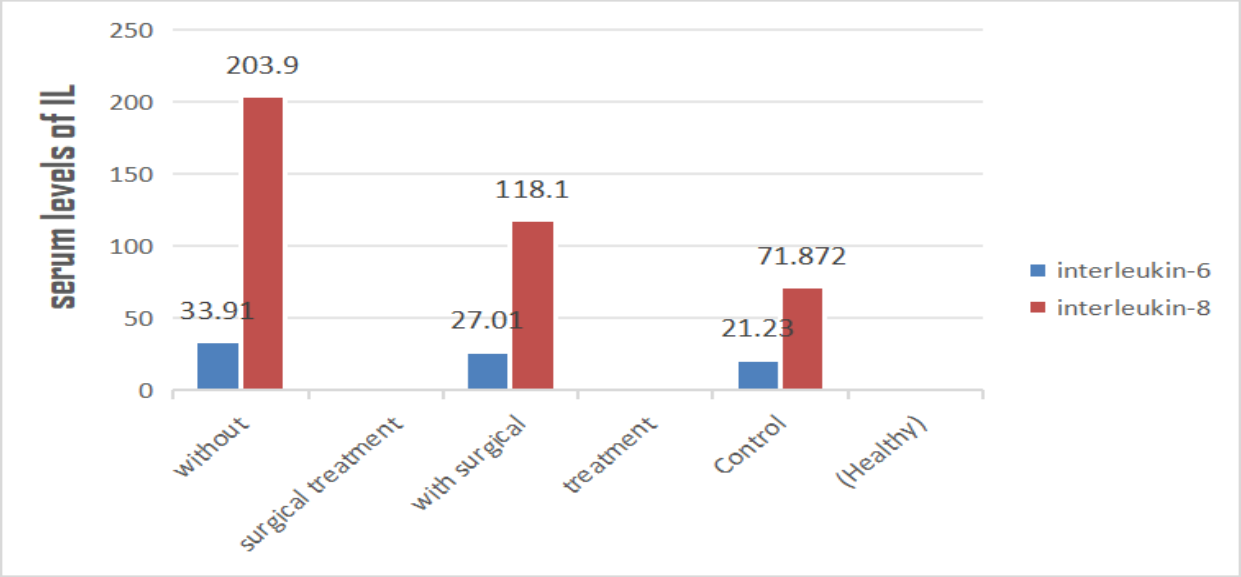

Figure (1): Serum levels of IL-6 and IL-8 in prostate cancer patients with surgical treatment

Discussion :

Prostate cancer tumor heterogeneity plays a critical role in shaping tumor immune responses, contributing to tumorigenesis [Shiao *etal.*, 2016)]. Elevated plasma levels of specific cytokines have been previously described in prostate cancer patients [Culig ,2021,Stanojković *etal.*,2020).the number of prostate cancer patients with surgical treatment (No.=60 , 60%) and without surgical treatment(No.=40 ,40 %).

Number of prostate cancer patients with surgical treatment was highest ($P < 0.05$) in the age group of 61≤ years (25 , 41.6%), followed by the age group of 51- 60 years (21 , 35 %)

serum IL-6 was significantly higher (33.91 ±2.81 pg/ml) in patients without surgical treatment as compared to patients with surgical treatment (27.01±3.31) However,Serum IL-8 was significantly higher (203.9 ±□3.82 pg/ml) in patients without surgical treatment as compared to patients with surgical treatment (118.10 ±□4. 99), Surgical Treatment such as radical prostatectomy , can lead to a decrease in IL-6 levels post-surgery, reflecting a reduction in tumor burden and inflammation. Similar to IL-6, IL-8 levels can be elevated in prostate cancer. IL-

8 is involved in angiogenesis and metastasis, and higher levels are often linked to poor prognosis.so the Post-surgical changes in IL-8 levels can vary. Some studies show a decrease in IL-8 after surgery, while others indicate that levels may remain elevated depending on the patient's overall health and cancer stage.

According to Culig *et al.,* there was a correlation between poor disease outcome and tumor differentiation and elevated levels of IL-6 in prostate tumors and the tumor microenvironment [Culig and Puhr, 2018]. Comparing primary and metastatic prostate cancer patients to healthy controls, Maynard *et al., f*ound that IL-8 was a cytokine that was expressed at higher levels in the former group [Maynard et al., 2019].

According to several researchers, there is a favorable link between preoperative levels of IL-1, IL-3, and IL-6 in patients with prostate cancer and those with malignant prostate diseases (Edward, 2004; Artus, 2009 and Mongiat-Artus *etal.*,2019]. Before and after surgery, there was a favorable correlation between the serum levels of the iterleukins IL-3, IL-4, and IL-5 in patients with prostate cancer. After four weeks of surgical therapy, we found elevated blood levels of IL-2 and IL-5 [Smith *etal.*,2007].

Ma *et al.* reported elevated serum levels of the cytokines IL-6 and TNF-α in patients with prostate cancer compared with controls, and this was associated with disease stage, PSA level and the presence of metastatic disease [Ma D *etal.*,2015]. For those individuals, the slight rise in IL-6 levels may result in a pro-inflammatory state brought on by chemotherapy, which includes fever, exhaustion, and "local" tumor discomfort [Messmann *et al. ,2003*].

Conclusion: Both IL-6 and IL-8 are important biomarkers in the context of prostate cancer. Their levels can provide insights into disease status and treatment response. Monitoring these cytokines may help in assessing the effectiveness of surgical interventions and in understanding the underlying inflammatory processes in prostate cancer patients.

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