

Estimation of IL1 Beta levels among UTI patients infected with cancer and without cancer

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Abstract

Methods: Our study was conducted from October 2024 to February 2024 from Salah Al-Din Oncology Centre, AL-Amal National Cancer Hospital and Teaching Oncology Hospital/Medical City, in Iraq. The study included urine samples collection (for use in culture to obtain bacterial isolates) and blood (for use in culture to obtain the serum to estimate interleukin- 1 beta) from 84 UTI patients with breast cancer, bladder cancer and prostate cancer (patient group) and 20 UTI patients without cancer (positive control group). in addition to 10 healthy people(negative control group). **Objective:** The study aims to investigate the diagnostic importance of interleukin-1 beta (IL-1 β), a promising biomarker for distinguishing UTI patients infected with cancer and without cancer and healthy controls. **Results:** The present study shows a decrease in the concentration of IL-1 β in UTI patients infected with cancer(patient group) compared to the UTI patients without cancer(positive control group) and healthy controls (negative control group). Four bacterial species were shown in this study. **Conclusions:** The decrease in concentration of IL-1 β in UTI patients infected with cancer(patient group). Bacterial species affect the concentration of IL-1 β in UTI patients infected with cancer (patient group) within a specific type of cancer .

Keywords: UTIs , IL- β , cancer types, without cancer.

1. INTRODUCTION

Urinary tract infections (UTI) are among the most common microbial disease in the world, which occurring in both public and healthcare settings. despite the clinical symptoms of UTIs are heterogeneous and range from simple (UTIs) to complex (UTIs), most UTIs are treated empirically. Bacteria are the common cause of UTIs , other microorganisms such as fungi and some viruses, have occasionally been implicated in UTIs[1]. UTIs encompasses various of clinical phenotypes, including cystitis, prostatitis, urosepsis, pyelonephritis and catheter-associated UTI (CA-UTI) [2]. UTIs are a common illness in people with solid cancers. While sustained and profound neutropenia from chemotherapy is uncommon, various variables enhance colonization of bacterial infection in patients with solid malignancies. Multiple risk factors are frequently associated. Specific considerations in this population include urine stasis due to tumor growth, alteration of These infections may be exacerbated by the increased use of medical apparatus, immunosuppression from anti-cancer therapy, and anatomical barriers.As multi-resistant germs arise, the epidemiology of illnesses alters, and polymicrobial infections become more common

[3]. In human, urinary tract infections (UTI), inflammation of the urinary system, which is characterized by recurrent and uncomfortable urination and occurs by the existence of bacteria, most commonly bacteria, in both the bladder and urethra. Simple or severe illness may result from a urinary tract infection[4]. UTIs are a significant clinical concern that accounts for 1–6% of referrals. In various environments, urinary tract infections (UTIs) are the most prevalent bacterial ailments.

One of the most common illnesses in people with solid cancers is urinary tract infection (UTI). While deep and protracted neutropenia brought on by chemotherapy is uncommon, a number of factors raise the risk of infection in patients receiving treatment for solid tumors, and it is not unusual for many risk factors to be associated. Additionally, several aspects were described in this particular population, including immunosuppression subsequent to anti-cancer therapy, alteration of natural anatomical barriers, and urine stasis secondary to blockage brought on by tumor development [6]. These infections might be encouraged by the growing use of medical equipment. As multi-resistant bacteria proliferate and polymicrobial diseases become more common, the epidemiology of these infections shifts with time. It is necessary to create novel therapeutic or even preventive strategies due to their severity and frequency in a particularly vulnerable group [7].

UTIs are followed by inflammation, which encompass several cytokines, including $\text{TNF-}\alpha$, interleukin (IL)- 1β , IL-6, and IL-8 [8]. The inception of interleukin-1, also known as IL-1, occurred in the 1940s when researchers first documented the pyrogenic properties of "soluble factors" produced by leukocytes triggered by endotoxins. Since that time, the scope of IL-1 research has expanded to encompass studies on inflammatory cytokines, Toll-like receptors (TLRs), innate immune responses, the identification of inflammasomes, and the therapeutic advantages of anti-IL- 1β treatment [9]. The two agonists that make up interleukin-1 (IL-1) are interleukin- 1α (IL- 1α) and interleukin- 1β (IL- 1β). They attach to IL-1 receptor 1 (IL-1R1) and use another peptide chain to initiate signalling[8]. The structures of IL- 1α and IL- 1β are similar and act similarly, although their amino acid sequence homology is very low (27%). Both have a core β barrel structure with neighboring loops and react with the IL-1R1 [10]. Two IL-1 agonists may be present for different reasons, such as their varying robustness or distinct roles [11]. A cytokine called IL- 1β stimulates inflammation as part of the immune response. Multiple cell types, including immune cells like macrophages & monocytes, as well as non-immune cells like epithelial and cancer cells, produce IL- 1β . Dysregulated inflammation and the severity of UTI have been linked to IL- 1β which is a potent pro-inflammatory cytokine [12]. Inflammatory signals trigger interleukin 1β of a wide range of immune cell types [13]. Monocytes and macrophages mainly secrete IL- 1β . It damages the tissues and allows neutrophils to enter it. A molecular complex called the inflammasome regulates and influences the production of the active form of IL- 1β to prevent uncontrolled inflammation [8]. The 269-amino acid precursor protein IL- 1β is manufactured and processed by caspase-1, sometimes referred to as the interleukin- 1β -converting enzyme (ICE), which is activated in inflammasomes. The final product of this processing is mature IL- 1β , which has 153 amino acids at its C-terminus [14]. Elevated IL-1 levels have been identified in a variety of solid tumours, including colon, breast, lung, and neck and head malignancies, which are associated with a worse prognosis. Immune cells, angiogenesis, cancer cell proliferation, migration, and metastasis are all impacted by IL-1 in cancer. Leukocytes are the main source of (IL 1β) stimulates the immune system at the site of inflammation or infection. Then, IL 1β is essential for the tumor inducing activities of

numerous malignancies, such as digestive tract tumours, as tumor-promoting inflamed is a hallmark of cancer. However, depending on the immune cell subtypes that react and infiltrate the tumor location, IL-1 β can have beneficial effects against tumours by initiating and attracting immune system cells to the tumour microenvironments [15]. Through signals between the immune and cancer cell populations, the infiltrating In the so-called tumour immune microenvironment, white blood cells or immune cells that reside within the tumours establish a biological niche that interacts with the cancer cells. Depending on the immune cell subtypes and the "media" of communication, this interaction between cancer cells and immune may control the growth and decline of malignancies. For decades, there has been debate regarding the pro- or anti tumorigenic effects of (IL-1 β), which is known in the context of innate immunity in tissues, play an important role in the signalling of inflammation. IL-1 β may have anti-tumour effects via stimulating phagocytes and antigen presenting cells [16]. Additionally, cancer treatments can stimulate the creation of IL-1 by immune or cancer cells, which has the opposite effect on the progression of cancer [17].

2 .MATERIAL AND METHODS

2.1 Samples collections

The present study included sample collection from October 2024 to February 2025 at Salah Al-Din Oncology Center, Tikrit, AL-Amal National Cancer Hospital and Teaching Oncology Hospital/Medical City, Baghdad, in Iraq .

2.1.1 Urine Samples Collection

The study included collecting 84 urine samples and blood samples from UTI patients infected with cancer (breast cancer, bladder cancer and prostate cancer) and considered as patient group and 20 urine samples from UTI patients without cancer and considered as positive control group.

2.1.2 Blood samples collections

40 Blood samples were collected from all patient who gave urine samples of both UTI patients infected with cancer (breast cancer, bladder cancer and prostate cancer) and UTI patients without cancer . Addition to ten blood samples were obtained from healthy people from healthy people (patients without UTIs , without cancer and without any infections) and considered as negative control group.

2.2 METHODS

All urine samples were cultured on selective and differential media (MacConkey agar and Blood agar) to isolate and purify bacterial species causing UTIs, and incubated them at a temperature of 37 for 24 hours then diagnosis confirmed by the use The VITEK2 system [18].

Blood samples were taken for measuring serum IL-1 β were only . By phlebotomist, four milliliters of blood were taken by a disposable syringe from the venous blood in highly sterile conditions and the blood samples were placed in special test tubes (gel tubes) and then the serum was obtained by centrifuging the sample at an approximate speed of 3000 (rpm) /minute for a ten minutes. Subsequently, the serum was meticulously transferred to eppendroph containers and preserved [19].

2.2.1 Identification of bacteria by using an automated technique

The VITEK2 mechanism: Automated techniques are highly precise and effective in the identification of microorganisms .The VITEK2 system comprises plastic reagent cards containing minute quantities of various biochemical test media in 30 wells. The biochemical profile obtained from these wells is

employed to diagnose living organisms. After the inoculum is introduced from cultivated samples into the card, a photometer periodically detects the colour changes in the card that are caused by the microbe's metabolic activity. The information was meticulously reviewed and efficiently stored in an electronic database. Numerous cards are accessible, including those for Gram-positive identification (GP) and Gram-negative identification (GN) [20].

2.2.2 Evaluation of IL-1 BETA level by ELISA test

Test Principle: This test employs the Sandwich enzyme immunoassay as its test principle. The microtiter plate that is included in this kit is pre-coated with an antibody that targets Interleukin 1 Beta (IL-1 β). A biotin-conjugated antibody that selectively targets IL-1 β is introduced after the addition of standards or samples to the appropriate microtiter plate well. Then, like a scientist meticulously carrying out an experiment, Each microplate well is incubated after Avidin, which is conjugated to {HRP} is applied. The addition of the TMB substrate solution will result in a colour shift in the wells that contain IL-1 β , biotin-conjugated antibody, and enzyme-conjugated Avidin. The enzyme substrate reaction concludes with the addition of a sulphuric acid solution and the subsequent measurement of the resulting colour shift. The enzyme-substrate reaction is halted by the addition of a sulphuric acid solution. The resulting colour change is subsequently determined by spectrophotometry at an emission wavelength of approximately 450 nm $\pm$ 10 nm. The quantity of IL-1 β present in the samples is determined by comparing the OD of the samples to the standard curve [21].

3. Results

In Table 1, the Results of the current study showed that there was lower significant in the concentration of IL-1 β (pg/ml) in the patient group compared with the positive control group and the negative control group ($P < 0.05$). In Table(2), according to the types of cancer, the results showed that was significant in IL-1 β (pg/ml) concentration in breast cancer and bladder cancer compared with prostate cancer ($P \leq 0.05$). which no significant difference in the concentration of IL1 β (pg /ml) was observed in prostate cancer ($P > 0.05$) of patients group compared with positive control group ($P \leq 0.05$). According to the types of bacterial isolates, there were highly significant differences in the concentration of IL-1 β (pg/ml) in all types of bacterial species in the patient group compared with the positive control group. In Table(3), according to Age, there were highly significant differences in the concentration of IL-1 β (pg/ ml) in the patient group and positive and negative controls ($P < 0.05$). There was no significant difference in the concentration of IL- 1 β (pg /ml) among the patient groups ($P > 0.05$). In Table(4), According to the Gender, there were highly significant differences in the concentration of IL-1 β (pg/ml) in patients group and positive control and negative control($P < 0.05$).

Table (1): concentration of IL -1 β (pg/ml) in patients group(UTI patients with cancer) , positive control(UTI patients without cancer) and negative control(patients without UTI and without cancer).

IL 1 β pg/ml	Cancer types and control				Negative control 10
	Bladder 27	Prostate 9	Breast 48	Positive Control 20	
Mean	C 26.43	C 24.13	D 20.08	B 32.53	A 40.40
Std. Error of Mean	1.99	2.82	0.91	2.81	3.51
Median	23.38	22.26	18.80	30.78	36.95
Std. Deviation	6.59	6.91	2.72	11.23	8.59
Minimum	18.80	16.77	17.78	19.00	34.39
Maximum	36.96	35.00	23.66	32.53	56.79
P value	0.05			0.002	0.001

LSD test was used to calculate the significant differences between the tested means, the letters (A, B, C and D) represented the levels of significant, highly significant starting from the letter (A) and decreasing with the last one.. Values of $p > 0.05$ were considered statistically non-significant, while $p \leq 0.05$ were considered significantly different

Table (2): Bacterial types and cancer types associated with IL1 β (pg/ml) concentrations in patients' group (UTI patients with cancer), positive control (UTI patients without cancer).

Bacterial Types Associated with IL 1 β pg/ml value	Cancer types and control				P value 1	P value 2
	Bladder 27	Prostate 9	Breast 48	Positive Control 20		
	Mean $\pm$ SD	Mean $\pm$ SD	Mean $\pm$ SD	Mean $\pm$ SD		
<i>E.coli</i>	D 19.82 $\pm$ 1.3	C 23.6 $\pm$ 1.1	B 28.6 $\pm$ 6.3	A 32.61 $\pm$ 4.3	0.002	0.05
<i>P.aeruginosa</i>	C 26.8 $\pm$ 2.1	B 32.1 $\pm$ 3.1	C 25.66	A 40.5 $\pm$ 2.9	0.001	0.04
<i>K.pneumoniai</i>	B 25.3 $\pm$ 4.8	A 33.2 $\pm$ 2.9	B 23.8 $\pm$ 2.1	A 32.66	0.05	0.001
<i>S.aureus</i>	24.01 $\pm$ 2.6	23.8 $\pm$ 4.7	24.5	36.2 $\pm$ 5.1	0.03	0.72
P value	0.05	0.09	0.05	0.05		

LSD test was used to calculate the significant differences between the tested means, the letters (A, B, and D) represented the levels of significant, highly significant starting from the letter (A) and decreasing with the last one.. Values of $p > 0.05$ were considered statistically non-significant, while $p \leq 0.05$ were considered significantly different

Table (3): according to Age , Mean of IL-1 β (pg/ml) between in patients group(UTI patients with cancer), positive control (UTI patients without cancer) and negative control(patients without UTI and without cancer).

Tested factors	Cancer types			Positive Control	Negat control
Age	*Bladder 27	Prostate 9	Breast 48	Control 20	10
Mean	58.20	59.50	55.53	36.75	39.0
Std. Error of Mean	1.94	2.31	1.71	1.96	5.6
Median	55.00	58.00	55.50	37.00	36.5
Std. Deviation	9.70	9.26	9.66	7.83	13.8
Minimum	35.00	44.00	22.00	23.00	26.0
Maximum	76.00	76.00	71.00	50.00	65.0

*P value between tested groups and + , - control **0.001** sig/p value between tested group only **0.87** non-sig/P $\leq$ 0.05 is considered statistically significant

Table (4): According to Gender, Mean of IL-1 β (pg/ml) between in patients' group(UTI patients with cancer), positive control (UTI patients without cancer) and negative control (patients without UTI and without cancer).

Gender	Cancer types and control				
	Bladder 27	Prostate 9	Breast 48	Positive Control 20	Negati control
Male N(%)	10(37.04)	9(100)	17(35.5)	10(50)	7(71)
Female N(%)	17(62.96)	0	31(64.5)	10(50)	3(30)
P value	The Fisher's exact test statistic is 8.64The p-value is 0.02 The result is significant at $p < 0.05$.				

4. Discussion

IL-1 β , or interleukin 1 beta, is a crucial proinflammatory mediator that appears in the early stages of bacterial infections and (UTIs) which are among the most prevalent bacterial illnesses. Therefore, IL-1 β is serving as a key mediators in the inflammatory response to UTIs [22]. In this study, IL-1 β was selected for examination because to its early manifestation in the immune system's response cascade and its presence in bodily fluids, including serum. The evaluation of IL-1 β in urinary tract infections is clinically viable and potentially beneficial due to its role in systemic inflammatory processes. The findings of the current study underscore uropathogenic bacteria that stimulate the production of the known as IL-1 β by glomerular endothelial cells, macrophages and interstitial tissue epithelial cells, which exhibited elevated levels of IL-1 β in the bacterial urinary tract infection group, corroborating with previous research that showed high level of IL-1 β in bacterial infections of UTIs group [24][25] [26] . According to the reports, anti-tumour theranostics drugs reduce inflammatory immune responses of IL 1 β and downregulate IL-1 β gene expressions in cancer[27] [28]and which agrees with results of this study. Results of this study recommend that themeasurement of IL-1 β level gives It serves as a thorough and effective reference for diagnosing urinary tract infections in patients and allows for the monitoring of microbial alterations in their serum. Moreover, cytokine IL-1 β is promising biomarkers for providing the possibility of early monitoring and detection of UTIs patients.

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