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Evaluating the Role of Biomarkers in Catheter-Related Urogenital Infections

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Abstract

Background: One of the most common infections acquired in the hospital setting is urinary tract infections (UTIs) associated with catheterization. Indwelling urinary catheters are used recurrently in older people.

Objective: Evaluate the diagnostic levels of the cytokines IL-6, TNF-α, IL-8, and calprotectin in the analysis of catheter-related urogenital infection, by using ELISA.

Subjects and Methods: Throughout the period between December 2024 to April 2025, 50 samples were collected serum from patients with diabetes foot surgery with renal failure and 50 serum from healthy person. The participants in this study ranged in age from 51 years and attended the hospitals of the Al-Dwiayniah Health Directorate. Both patient and control three milliliters of venous blood were collected by syringes, then placed in gel tubes and centrifuged at 3000 rpm for 10 minutes, and serum was dispensed into 2 Eppendorf tubes and they were kept at -20°C until testing. ELISA was charity to quantify the absorptions of TNF-α, IL-8, IL-6, and calprotectin.

Results: The results showed the Mean levels of Interleukin-6 were 223.53 ± 21.3 in patients compared with 78.53 ± 11.6. whereas Mean levels of Interleukin-8 were 41.11± 4.63 in patients' comparison with control 18.90 ± 4.3. Also, the results show the Mean levels of Interleukin TNF-α were 265.83± 15.3 in patients compared with 118.73 ± 11.61. whereas Mean levels of Interleukin calprotectin were 375.04± 38.29 in patients compared with 169.67 ± 21.35. The mean flat was greatly higher than in urinary catheters sick in comparison with well-controlled (P< 0.001).

Conclusion: The results revealed an increased rate of disease in males, 161 (80.5%), in comparison with females, 39 (19.5%). Also, significantly great serum levels of IL-6, TNF-α, IL-8, and calprotectin in catheterization patients compared to patients who do not have catheter-associated urinary tract infections (CAUTIs).

Keywords: catheter-related urogenital infections, calprotectin, IL-6, IL-8, TNF-α, ELISA.

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INTRODUCTION

A catheterized sick curiously high urine bacterial count has been designated as a catheter-related urinary tract infection (CAUTI). A urinary catheter can allow bacteria or other microorganisms to enter the urinary tract and cause CAUTI. CAUTIs have been linked to higher rates of morbidity, mortality, length of stay, and medical expenses. Catheter-associated asymptomatic bacteriuria (CA-ASB), which lacks urinary tract-related expression or declaration, and CAUTI with urinary tract-related manifestations are the two categories into which it can be broadly divided. UTIs acquired through medical devices account for up to 40% of hospital-acquired infections, making them one of the most prevalent infections acquired in healthcare settings[1,2].

Alternatively, Fletke et al. 2024 stated that certain symptoms i.e. CAUTIs, are characterized by chills, fever, urine leakage around the catheter, pressure on the catheter, and pain and discomfort in the lower posterior or stomach. If the patient is not treated and the catheter is left in place for an extended period, kidney damage, pyelonephritis, and even septicemia may result. Miriam and associates.[3] revealed that a living microbe (M. O) such as Lactobacillus, Enterococcus, Bifidobacteria, and Saccharomyces cerevisiae, which are common human flora, are thought to have positive health effects when taken or applied topically; this is known as a probiotic. Humans benefit from probiotic M.O., which can inhibit Staphylococcus species. and other human infections through a variety of mechanisms, such as enhancing the function of the uro-epithelial barrier and boosting the immune response by communicating with immune system cells through a small number of antigen-presenting cells. Additionally, there is proof that probiotics can stop pathogens from colonizing. This can be accomplished through mechanisms like inhibiting pathogen adherence and down-regulating Staphylococcus virulence factors that cause biofilm formation[4,5].

Many different types of cells release tiny proteins called cytokines in response to inflammation and infections. An essential mediator of the acute phase response in the early stages of bacterial infection is the pro-inflammatory cytokine interleukin-6[6]. Interleukin-8 is produced through macrophages and endothelial cells and productions a major role in migrating neutrophils to the location of inflammation and prompting phagocytosis once they have entered the site of inflammation[7]. During the acute phase of UTI, increased serum concentrations of IL-6 and IL-8 were observed. So, cytokines and acute-phase inflammatory cells synergistically respond to inflammation caused by UTI. The authors also conclude that UTI cytokine responses differ according to infection severity and host diversity, and that the fragile nature of the bacteria may influence cytokine activation[8].

A calcium-binding complex consisting of two proteins belonging to the so-called S100 group (S100A8/S100A9) is called calprotectin. It contributes up to 60% of the cytosolic proteins in neutrophil cytoplasm and is mostly released by neutrophils and, to a lesser extent, by monocytes[9]. Calprotectin is a natural immune system activator. When an invading microorganism stimulates a neutrophil granulocyte, it releases calprotectin in the form of a damage-associated protein (DAMP). Calprotectin activates Toll-Like Receptor 4 (TLR4), thereby increasing the inflammation potential. Calprotectin is a promising candidate biomarker for UTI based on its origin and physiological role in the treatment of traumatic encephalitis. Urine calprotectin, an activated innate immune system mediator, is used as a marker for various inflammatory conditions[10]. TNF-α remains a cytokine that distresses diverse kinds of cells in a pleiotropic way. The pathophysiology of certain inflammatory and autoimmune diseases is known to involve it, and it has remained recognized as a crucial controller of inflammatory reaction[11]. Natural killer cells, T-lymphocytes, and stimulated macrophages are the main producers of TNF-α, a homotrimer protein consisting of 157 amino acids[12]. To our knowledge, this is the inaugural study of its kind in Iraq. Researchers are investigating the diagnostic efficacy of a few immunological biomarkers in urogenital infection patients who have catheters.

MATERIALS AND METHODS

Before being used, completely substances, regular solutions, and testers were ready by the kit's instructions and allowed to come to room temperature. The regular bores were full with 50µl of the regular sequential dilution. Meanwhile, the regular solution comprises biotinylated antibody; no further antibody is supplementary to the regular ones. After adding 40µl of the sample to each well, 10µl of the anti-antibody remained supplementary, and 50µl of streptavidin-HRP was added to both the sample wells and the standard well (not the blank control well). After thoroughly mixing the

ELISA, a sealer stayed practical to the plate. Then keep warm at 37°C for 60 minutes. Next, eliminating the sealer, the platter was pounded in five intervals using a shower buffer. For every shower, bores stood saturated in at least 0–35 ml of shower buffer for 30–1 minute. Every bore was first filled with 50µl of substrate solution A, and subsequently with 50µl of substrate B. Next, relating to a fresh sealer, the platter was left in the dark at 37°C for ten minutes. After adding 50µl of End Solution to every bore, the blue color will instantly turn yellow. Within ten minutes of adding the end solution, the optical density (OD value) stayed stately by a microplate reader fixed to 450 nm.

INTENTION OF OUTCOMES

Each standard's and sample's optical density readings were used to calculate the ELISA results. The standard curve was then plotted against the concentration on the Y-axis by the mean OD rate for every regular interval on the X-axis, and a fine fitting curve was formed through connecting the graph's points.

Statistical analysis:

Microsoft Office Excel 2010 and SPSS version 26 were used to create, accumulate, analyze, and present data. Statistical tests, including t-tests, chi-square examinations, and ROC curve investigations, were employed to analyze the data.

ETHICAL CONSIDERATION

The research was carried out in compliance with ethical standards, and consent was obtained from the patient or the patient's family before taking the sample. The study was conducted confidentially; moreover, this study was not disclosed, and the participation of patients was optional. The study system and approval form were reviewed by the Ethics Committee at the system, and the agreement formula was revised via the Ethics Commission at the College of Medicine, University of Al-Qadisiyah.

RESULTS

Interleukin-6 (IL-6) levels were compared between patients who had urinary catheters and well-controlled matters; the outcomes are displayed in Table 1, also in Figure 1. As soon as paralleling sick with urinary catheters to well-controlled, the mean levels of Interleukin-6 stayed considerably greater in the former grouping (P<0.001), with mean levels of 223.53 ± 21.3 and 78.53 ± 11.6 in the former group, respectively.

Table 1. level of interleukin-6 (IL-6) in healthy controls and patients.

Groups		(IL-6) level
Urinary catheters patients	Mean ± SD	**223.53 ± 21.3**
	Range	159.65-336.80
Control	Mean ± SD	**78.53** ± 11.6
	Range	36.02-129.33
p-value		**< 0.001** † S

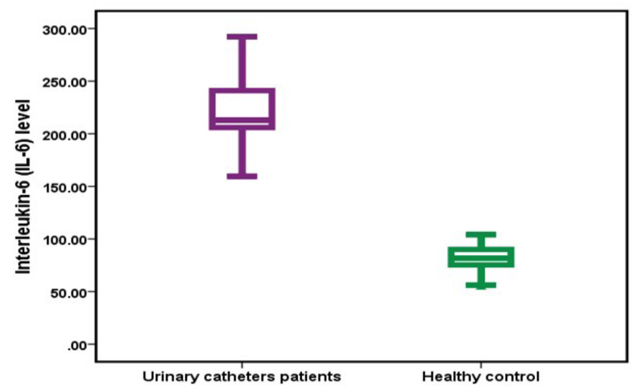

Figure 1. Mean IL-6 ranks of sick and well control Assessment of Interleukin-6 (IL6) ranks

(ROC) Curve examination was used to assess the IL-6 cutoff rate and expect urinary catheters as prognostic or adjuvant prognostic examinations. The findings are presented in Table 2 also in Figure 2. Through sensitivity (NPV), specificity (PPV), and zone below the curve of 100.0%, 100.0%, 100.0, and 1.000 (1.000-1.000), the IL-6 cutoff value was >244.49-fold. According to the existing findings, IL-6 is considered a highly reliable prognostic indicator.

Table 2. Sensitivity and specificity of IL-6 (> 244.49-fold) in urinary catheters

Interleukin-6	Patients *n* = 50	Well control *n* = 50
> 244.49	50	0
> 244.49	0	50
Sensitivity %	100%	
PPV %	100%	
Specificity %	100.0 %	
AUC(95%CI)	1.000 (1.000- 1.000)	
NPV %	100.0 %	

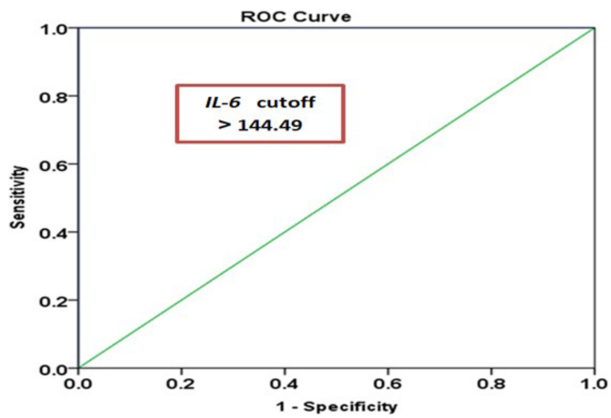

Figure 2. ROC curve examination of IL-6 for the screening of a potential prognostic cutoff value.

Interleukin-8 (IL-8) level in patients with urinary catheters and healthy controls.

Interleukin-8 (IL-8) levels were compared between sick patients who had urinary catheters and well control matters; the findings are displayed in Table 3 and Figure 3. When comparing sick individuals with urinary catheters to well controls, the mean levels of Interleukin-8 were considerably higher in the former grouping (P<0.001), with mean levels of 41.11 ± 4.63 and 18.90 ± 4.3 in the former group, respectively.

Table 3. IL-8 flat in sick and well control.

Groups		Interleukin-8 (IL-8) level
Urinary catheters patients	Mean ± SD	**41.11 ± 4.63**
	Range	23.60-47.40
Control	Mean ± SD	**18.90** ± 4.3
	Range	6.78-26.10
p-value		**< 0.001** † S

EVALUATION OF INTERLEUKIN-8 (IL-8) LEVELS

An analysis of the ROC curve was performed to assess the IL-8 (IL-8) cut-off value and to predict urinary catheters as prognostic tests or adjuvant examinations, and the outcomes are presented in Table 4, besides Figure 4. Index value of IL-8 was >26.05-fold with sensitivity (PPV), specificity, (NPV), and zone below the curve (AUC) of 98.0, 100.0, 100.0, and 0.992 (0.975-1.000). The existing outcomes indicate IL-8 is reflected as a tremendous prognostic marker.

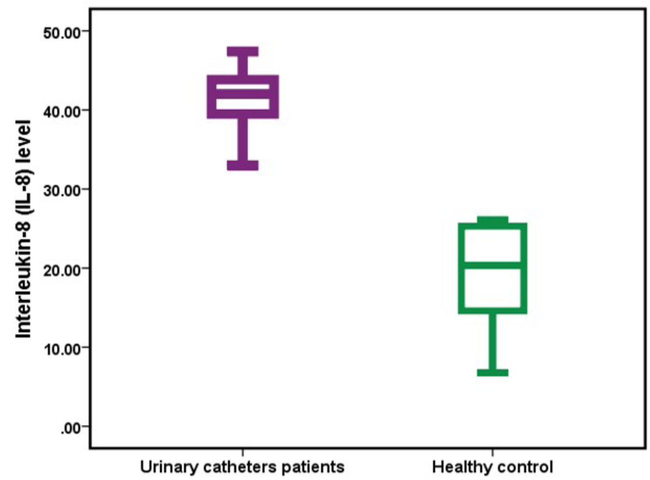

Figure 3. Mean IL-8 ranks of sick and well controls

Table 4. Sensitivity and specificity of IL-8 (> 26.05-fold) in urinary catheters

Interleukin-8	Patients $n = 50$	Healthy control $n = 50$
> 26.05	49	0
> 26.05	1	50
Sensitivity %	98%	
PPV %	98%	
Specificity %	100%	
AUC (95%CI)	0.992 (0.975- 1.000)	
NPV %	100.0 %	

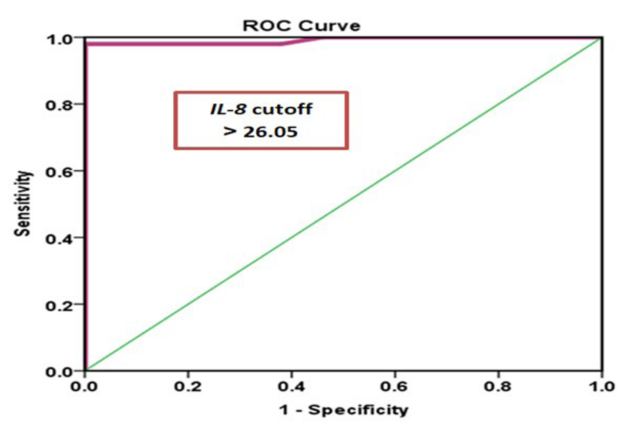

Figure 4. ROC curve investigation of IL-8 for the screening of a possible prognostic cutoff rate.

TNF-α flat in sick patients with urinary catheters and well-controlled.

A comparison of the levels of (TNF-α) between urinary catheter sick and well-controlled subjects was conducted, and the results are revealed in Table 5 and Figure 5. When comparing sick with urinary catheters to well-controlled, the mean levels of TNF-α stood considerably upper in the former group (P< 0.001), with mean levels of 265.83 ± 15.3 and 118.73 ± 11.61, respectively.

Table 5. TNF-α flat in sick and well control.

Groups		(TNF-α) level
Urinary catheters patients	Mean ± SD	**265.83 ± 15.3**
	Range	245.50-293.20
Control	Mean ± SD	**118.73** ± 11.61
	Range	93.50-161.70
p-value		**< 0.001** † S

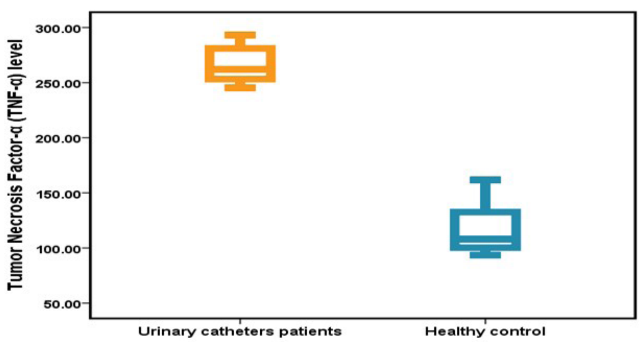

Figure 5. Mean TNF-α levels of sick and well controls

Evaluation of Tumor Necrosis Factor-α (TNF-α) level.

ROC Curve examination remained a method to gauge the TNF-α cutoff rate and expect urinary catheters as prognostic or adjuvant prognostic examinations. The fallouts are presented in Table 6, besides Figure 6. With PPV, sensitivity, specificity, NPV, and zone below the curve of 100%, 100%, 100%, and 1.000 (1.000- 1.000), the TNF-α cutoff value was >203.55-fold. According to the current findings, TNF-α is regarded as a highly reliable prognostic indicator.

Table 6. Sensitivity and specificity of TNF-α (> 203.55-fold) in urinary catheters

TNF-α	Patients *n* = 50	Well control *n* = 50
> 203.55	50	0
> 203.55	0	50
Sensitivity%	100%	
PPV %	100%	
Specificity %	100%	
AUC (95%CI)	1.000(1.000- 1.000)	
NPV %	100.0 %	

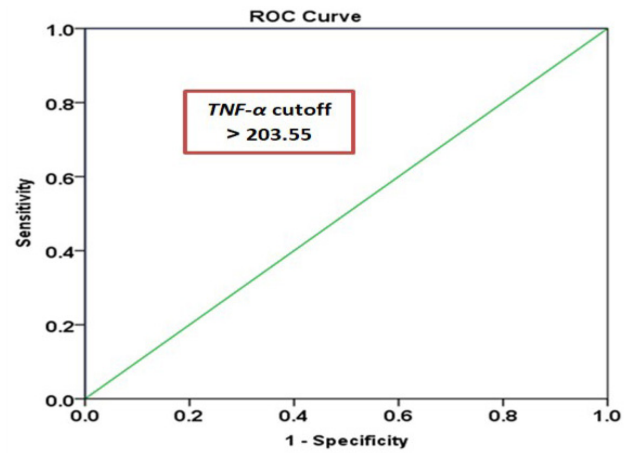

Figure 6. ROC curve investigation of TNF-α for the design of a possible prognostic cutoff rate.

Human Calprotectin flat in sick with urinary catheters and well-controlled

Patients with urinary catheters and healthy control subjects had their human calprotectin levels compared; the results are shown in Table 7 and Figure 7. Calprotectin levels in patients with urinary catheters were 375.04±38.29 and 169.67±21.35, respectively; the mean flat stayed significantly higher in urinary catheter sick than in healthy controls (P< 0.001).

Table 7. Hominid Calprotectin flat in sick and healthy controls.

Groups		Human Calprotectin level
Urinary catheters patients	Mean ± SD	**375.04 ± 38.29**
	Range	192.20-516.24
Control	Mean ± SD	**169.67** ± 21.35
	Range	59.00-251.50
p-value		**< 0.001** † S

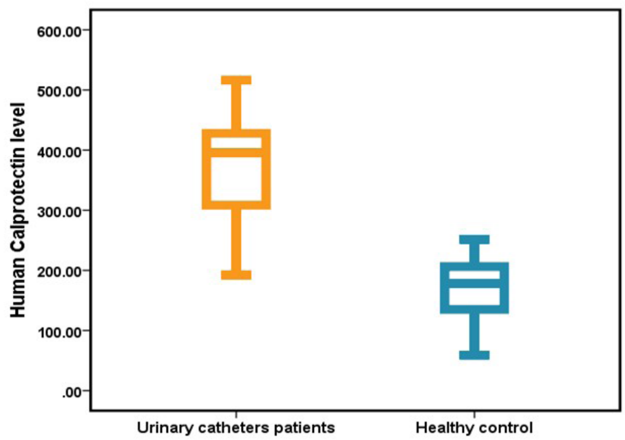

Figure 7. Mean Calprotectin levels of sick and well controls

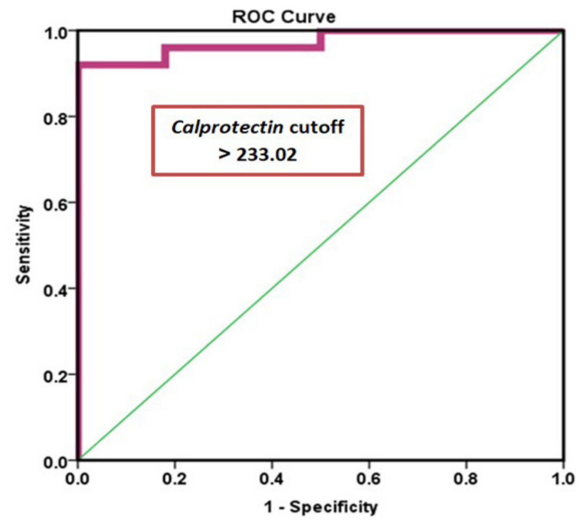

Figure 8: ROC curve examination of Calprotectin for the screening of potential prognostic cutoff rate

Evaluation of Human Calprotectin Level

To gauge the Calprotectin cutoff rate in addition to calculating urinary catheters as prognostic examinations or adjuvant prognostic tests, (ROC curve examination was carried out, and the outcomes are presented in Table 8, also in Figure 8. Calprotectin cutoff rate remained >233.02-fold with 98 sensitivity, PPV, specificity, NPV, and zone below the curve. 98%, 96%, 96.1%, 0.973%, and 0.943 percent (0.943-1.000). The present outcomes indicate that Calprotectin is reflected as a tremendous prognostic indicator.

Table 8. Sensitivity and specificity of Calprotectin (> 233.02-fold) in urinary catheters

Calprotectin	Patients *n* = 50	Healthy control *n* = 50
> 233.02	49	2
> 233.02	1	48
Sensitivity %	98.0 %	
PPV %	96.1 %	
Specificity %	96.0 %	
AUC (95% CI)	0.973 (0.943- 1.000)	
NPV %	98.0 %	

DISCUSSION

The grade of rise provisions the character of catheters in activating systemic inflammation. IL-6 is a crucial inflammatory cytokine raised in infection and tissue damage. Catheters augment contagion danger, which motivates IL-6 relief. This agrees with[13] who institute catheter related (CAUTI) had IL-6 levels>200 pg/mL, whereas non-catheter-associated urinary persisted <100 pg/mL. Furthermore to[15] designates an important rise in serum (IL-6) ranks in sick patients with austere renal inefficiency after catheterization. Also agrees with those who concluded urine cytokine reports could assist as a noninvasive assessment provision implemented in medical practice and contribute to anti-microbial stewardship[4]. But the outcome possible disagree with[16] who concluded the ranks of IL-6 stayed considerably related to hypertension, age, strictness, and mortality.

According to the existing findings, IL-6 is considered a highly reliable prognostic indicator. This consisted with[17] who concluded raised IL-6 levels, with a 100% sensitivity for analyzing diseases and propose that observing IL-6 might assistance to improve dialysis managing and progress the overall prediction of sick, in addition to, IL-6 displayed promising analytic accurateness across numerous illnesses, proposing it's possible as a consistent analytical biomarker in the adjacent upcoming. IL-6 has proven high indicative exactness across several illnesses, representative it's probable as a dependable biomarker in the future, supported by considerable evidence and proposed to contend that novel, more precise proteomic biomarkers might overtake IL-6 in forecasting kidney rescue[18].

IL-8 levels were considerably higher in catheterized sick patients, suggesting an inflammatory reaction related to catheter usage, that reliant with the elevated IL-8 levels in sick patients with urethral illness. IL-8 remains a pro-inflammatory chemokine produced in inflammatory situations through immune and additional cell types. Plasma IL-8 remains an encouraging indicator for the initial detection of severe kidney damage. Obstinate acute kidney damage progression concluded that IL-8 up-regulation might be owing to tubular damage, inflammation, and immune cell enrollment. Over-expression of IL-8 be able to cause tissue injury, whereas hindering it can opposite this consequence. Neutrophil dysregulation and extreme neutrophil extracellular traps can likewise facilitate tissue destruction. The investigation provisions the usage of IL-8 as an additional urine-specific biomarker in contagion-linked kidney damage. Additionally austere LUTS grade had upper serum IL-8 ranks related to a slight LUTS grade. Moreover, urinary IL-8 levels increased next a urinary catheter insertion[19].

According to the existing fallouts propose IL-8 is a highly precise predictive indicator for catheter-related difficulties, and raised circulating IL-8 relates to humble prediction in urological tumors. Also, the researcher concluded a rise in IL-8 ranks in response to pathogenesis. Moreover, the investigation provisions the usage of numerous urine biomarkers, including IL-8 with high sensitivity (90%) to improve analytical accuracy in UTI[20]. But disagree with those who concluded that a susceptible, however non-specific, broadcast biomarker for urinary tract illnesses might be urine IL-8 levels, which stay elevated in mutually diseased and non-infectious urinary tract difficulties. Likewise, serum IL-8 did not considerably alter among patients throughout the severe and the convalescing stage[21].

This rise might reveal an intensified inflammatory reaction owing to catheter related (CAUTIs). This agrees with those who concluded TNF-α levels are considerably augmented in the urine of catheterized sick when compared with the urine of non-catheterized well-presenting patients. Also, other outcomes propose that urine could be a worthy environment to gauge TNF-α alterations[18]. In addition to the serum and urinary levels of the TNF-α increases too furthermore, the plasma and urinary levels of the TNF-α have a straight and important association with each other. This proposes TNF-α remains a robust biomarker for forecasting catheter-related results. These outcomes are consistent with modern searches that determined that urinary TNF-α potency is a worthy marker for inflammatory reaction. TNF-α is considered a modulator of major diseases in order to highlight the vital interfaces existing in established inflammation. (TNF-alpha) It is an encouraging biomarker for forecasting the severity of many diseases and environments, and functional rescue from these acute conditions. Checking these cytokines in the initial phases of these circumstances could assist in recognizing patients at greater risk for long-term disease, possibly managing personalized treatment approaches[22].

The results indicate that calprotectin (CP) levels are considerably higher in patients with urinary catheters, possibly owing to enduring inflammation or infection related to catheter practice. This is consistent with[23], who proposed cooperative progress in regular recognition practices and advanced investigation methodologies. CP-based approaches are predictable to be combined into conventional medical training for sick with inflammatory diseases. Additionally, because CP is a cytosolic protein found in neutrophil granulocytes, it continues to be a marker of inflammation[24].

The existing result is reliable with[25], who concluded Serum Calprotectin Stays an effective Biomarker in recognition of bacterial UTI by ROC. Also, the CP test is a dependable indicator for considering sickness action and might have superior capability to consider sickness activity. In addition to studying the rate of CP as an analytical biomarker, founded on earlier training that established higher CP ranks in patients[26,27,28].

Conclusion: A significantly higher serum level of IL-6, TNF-α, IL-8, and calprotectin in catheterization patients compared to patients who do not have catheter-associated urinary tract infections (CAUTIs).

Ethics Statement and Conflict of Interest Disclosures

Financial support and sponsorship: All authors have declared that no financial support was received from any organization for the submitted work.

Ethics Consideration: The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national

laws. Written informed consent was provided by the patient participant in this study.
This study was approved by the Institutional Research Board and Ethics Committee.
Conflict of interest: No known conflict of interest correlated with this publication.
Availability of data and materials: The data used and/ or analyzed throughout this study are available from the corresponding authors upon reasonable request.
Competing interests: The authors declared that they have no competing interests.
The use of generative AI and AI-assisted technologies: The authors did not use in this article generative AI and AI-assisted technologies.

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