# Biochemical, Immunological, and Microbiological Profiles with Antimicrobial Resistance Patterns: A Comparative Analysis in Control, Hemodialysis, and Urinary Tract Infection Patients

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## Abstract

**Background: Urinary tract infections (UTIs) pose a significant health burden, particularly in vulnerable populations like hemodialysis patients who often face impaired immune function and increased exposure to healthcare environments. This study aimed to conduct a comprehensive comparative analysis of demographic, biochemical, immunological, and microbiological characteristics across healthy controls, hemodialysis patients, and non-dialysis patients with confirmed UTIs. The objective was to delineate distinct clinical and laboratory profiles, including antimicrobial resistance patterns, among these cohorts.**

**Methods: A cross-sectional study was performed involving three groups: ٣٥ healthy controls, ٣٥ patients undergoing maintenance hemodialysis, and ٣٥ non-dialysis patients diagnosed with UTIs. Data encompassed demographic details (age, sex, residence), biochemical parameters (creatinine, blood urea, fasting blood sugar), and immunological markers (IL-٦, IL-٨, IL-١٧). Microbiological assessment of urine samples from patient groups included bacterial identification and antibiotic susceptibility testing. Statistical analyses involved descriptive statistics, independent samples t-tests/Mann-Whitney U tests for continuous variable comparisons, Chi-square tests for categorical associations, and Pearson correlation for relationships among quantitative variables. Data visualization utilized bar charts, box plots, and heatmaps.**

**Results: The hemodialysis group showed significantly elevated mean levels of serum creatinine (٩,٢٢ ± ٠,٧٥ mg/dL), blood urea (١٥٠,٩٤ ± ٢٠,٧٥ mg/dL), and fasting blood sugar**

**(١٤٣,٧١ ± ٦٤,٢٠ mg/dL) compared to both control and UTI groups (p < ٠,٠٠١ for all). Immunological profiling revealed significantly higher mean IL-٦, IL-٨ and IL-١٧ levels in both hemodialysis and UTI groups compared to controls (p < ٠,٠٠١). Demographically, the hemodialysis group was older (mean age ٤٨,٦٩ years) and predominantly male, while the UTI group was younger and largely female. Recurrent UTIs were universally reported in hemodialysis patients (١٠٠٪) and common in the UTI group (٦٢,٩٪). *Escherichia coli* was the most common pathogen in both patient groups, but the hemodialysis cohort exhibited a broader diversity of pathogens including *Staphylococcus aureus* and *Pseudomonas aeruginosa*. A high prevalence of antimicrobial resistance, notably to Ciprofloxacin and Gentamicin, was observed across both patient groups. Strong positive correlations were found between creatinine and blood urea in all groups, and among IL-٦, IL-٨, and IL١٧ in patient groups.**

**Conclusion: Hemodialysis patients present a distinct and complex profile characterized by profound biochemical derangements, heightened inflammatory states, and a diverse spectrum of bacterial infections with significant antimicrobial resistance. These findings underscore the critical need for tailored monitoring, infection control, and antimicrobial stewardship strategies specifically designed for dialysis populations, taking into account their unique clinical and immunological vulnerabilities.**

**Keywords: Hemodialysis, Urinary Tract Infection, Inflammatory Markers, Cytokines, Antimicrobial Resistance, Pathogen Profile, Cross-Sectional Study, Biochemical Markers, Immune Dysregulation.**

## Introduction

Urinary tract infections (UTIs) represent a pervasive public health challenge, standing as one of the most common bacterial infections globally, contributing to millions of outpatient visits and hospitalizations annually and imposing a substantial burden on healthcare systems [١,٢]. While UTIs predominantly affect women and the elderly, their incidence, recurrence, and severity are significantly amplified in immunocompromised individuals and those with chronic comorbid conditions [٣,٤]. Among these vulnerable populations, patients undergoing maintenance

hemodialysis are at a particularly heightened risk of developing recurrent and severe UTIs [٥]. This unique susceptibility in hemodialysis patients is attributable to a confluence of factors, including an inherent state of immunosuppression, the necessity of long-term catheterization or vascular access, the high prevalence of coexistent conditions such as diabetes mellitus, and frequent exposure to healthcare environments where nosocomial pathogens may be prevalent [٦,٧]. The clinical consequences of these infections in end-stage renal disease (ESRD) patients are profound, contributing significantly to increased morbidity, hospitalization rates, and mortality [٨,٩]. Furthermore, the escalating global challenge of antimicrobial resistance exacerbates infection management in this already fragile population, as multi-drug-resistant (MDR) organisms are increasingly implicated in dialysis-associated infections [١٠,١١].

The assessment of renal function and metabolic status is critical in managing patients with kidney disease. Biochemical markers such as serum creatinine, blood urea (nitrogen), and fasting blood sugar are fundamental indicators providing insights into kidney efficiency and systemic metabolic regulation [١٢,١٣]. Elevated levels of creatinine and urea are classic hallmarks of impaired glomerular filtration rate and accumulated uremic toxins, which are characteristic features of ESRD [١٤,١٥]. Abnormalities in blood glucose levels are also common in ESRD patients, often stemming from underlying diabetes or insulin resistance, influencing both disease progression and susceptibility to infections [١٦,١٧]. Monitoring these biochemical parameters is thus essential for evaluating disease severity, therapeutic efficacy, and assessing the overall vulnerability of dialysis patients to infectious complications [١٨,١٩].

Beyond conventional biochemical markers, the host immune response plays a pivotal role in the pathogenesis and outcome of infections. Inflammatory cytokines, such as Interleukin-٦ (IL-٦), Interleukin-٨ (IL-٨), and Interleukin-١٧ (IL-١٧), serve

as crucial mediators of innate and adaptive immunity, reflecting the body's response to infection and inflammation [٢٠,٢١]. In chronic disease states like ESRD and active infections like UTIs, dysregulation of these immunological markers can contribute to compromised host defense and persistent inflammation [٢٢,٢٣]. A comprehensive understanding of these cytokine profiles can offer valuable insights into the immune status and inflammatory burden in different patient cohorts.

The microbiological landscape of UTIs in hemodialysis patients often diverges from that observed in the general population. While *Escherichia coli* remains the most common uropathogen across both community-acquired and hospital-acquired infections, dialysis settings frequently encounter a broader spectrum of organisms, including opportunistic and often drug-resistant strains of *Staphylococcus aureus* and *Pseudomonas aeruginosa*, as well as various *Klebsiella pneumoniae* isolates [٢٤,٢٥]. These infections present considerable therapeutic challenges, leading to prolonged hospital stays and increased healthcare resource utilization [٢٦,٢٧]. The high prevalence of recurrent UTIs in both non-dialysis and hemodialysis populations, though driven by distinct underlying risk factors (e.g., anatomical factors in general population versus catheter use and immunosuppression in dialysis patients), underscores the need for targeted preventive and management strategies [٢٨,٢٩].

Despite the substantial clinical impact of UTIs in hemodialysis patients, comprehensive comparative studies that simultaneously analyze demographic, biochemical, immunological, and microbiological features across healthy controls, hemodialysis patients, and non-dialysis UTI patients remain limited [٣٠]. Such integrated comparisons are crucial for elucidating distinct disease patterns, identifying specific biomarkers indicative of infection type and severity, and informing evidence-based clinical decision-making.

This study aims to bridge this existing gap by conducting a rigorous comparative analysis of demographic characteristics, routine biochemical parameters, a panel of inflammatory immunological markers, and detailed microbiological profiles, including antimicrobial resistance patterns, among healthy control individuals, patients undergoing maintenance hemodialysis, and non-dialysis patients diagnosed with UTIs. By integrating robust statistical analysis, including correlation modeling and comprehensive pathogen profiling, this research seeks to provide a deeper, multi-faceted understanding of the differences and similarities between these patient groups, thereby contributing to the development of more informed and tailored diagnostic, therapeutic, and preventive clinical practices.

## ٢. Methodology

### ٢،١ Study Design and Setting

This study was designed as a comparative cross-sectional investigation, meticulously conducted within a tertiary care center in Baghdad, Iraq, during a defined period. The study protocol was meticulously reviewed and approved by the institutional review board (IRB) of [Insert Institution Name/Ethics Committee, if available]. All participants provided informed consent (either verbal or written, as applicable and approved by the IRB) prior to their inclusion in the study.

### ٢،٢ Study Population

A total of **١٠٥ participants** were systematically included in the study, thoughtfully stratified into three distinct groups, each comprising ٣٥ individuals:

- **Group A (Control Group):** Consisted of ٣٥ apparently healthy individuals with no history of chronic diseases, renal impairment, or active infections, serving as a baseline for comparison.

- **Group B (Hemodialysis Group):** Comprised ٣٥ patients actively receiving regular maintenance hemodialysis treatment for end-stage renal disease.
- **Group C (UTI Group):** Included ٣٥ non-dialysis patients diagnosed with laboratory-confirmed Urinary Tract Infections (UTIs), with no prior history of renal replacement therapy.

**Inclusion criteria for all groups were:**

- Age ≥ ١٨ years.
- For patient groups (Hemodialysis and UTI), a laboratory-confirmed UTI with significant bacterial growth on urine culture at the time of sampling.
- Availability of complete demographic, biochemical, and relevant immunological data.

**Exclusion criteria for all groups included:**

- Presence of systemic infections other than UTI (for patient groups).
- Recent antibiotic use within the preceding ٧٢ hours (to minimize confounding effects on microbiological assessment).
- Known immunosuppressive therapy or diagnosed autoimmune diseases.
- Pregnancy.
- Any acute severe illness unrelated to their primary condition that could significantly alter biochemical or immunological parameters.

### ٢,٣ Data Collection

Data were comprehensively collected from each participant using a standardized, structured form. The collected variables were categorized as follows:

#### ٢,٣,١ Demographic Variables

- Age (in years)
- Sex (Male/Female)
- Residence (Urban/Rural)
- History of recurrent UTI (Yes/No)

- Family history of UTI (Yes/No, collected for Hemodialysis patients).

### ٢,٣,٢ Biochemical Parameters

Blood samples were collected following standard venipuncture protocols. Serum was separated, and the following parameters were measured using standard automated laboratory techniques at the hospital's central laboratory:

- Serum creatinine (mg/dL)
- Blood urea (mg/dL)
- Fasting blood sugar (mg/dL)

### ٢,٣,٣ Immunological Markers

Serum samples were processed for the quantification of key inflammatory cytokines. The following immunological markers were measured using [Specify method, e.g., Enzyme-Linked Immunosorbent Assay (ELISA)] according to manufacturers' protocols:

- Interleukin-٦ (IL-٦, pg/ml)
- Interleukin-٨ (IL-٨, pg/ml)
- Interleukin-١٧ (IL-١٧, pg/ml)

### ٢,٣,٤ Microbiological Assessment

For patients in the Hemodialysis and UTI groups, midstream clean-catch urine samples were collected under strict sterile conditions. Samples were immediately transported to the microbiology laboratory.

- **Culture:** Urine samples were cultured quantitatively on standard media including Blood Agar and MacConkey Agar plates. Plates were incubated aerobically at ٣٧°C for ٢٤-٤٨ hours. Significant bacterial growth was defined as ≥١٠٥ Colony Forming Units (CFU)/mL.
- **Bacterial Identification:** Isolated bacterial organisms were identified to the species level using conventional biochemical tests (e.g., API ٢٠E/API Staph, VITEK ٢ system) and morphological characteristics.

- **Antibiotic Susceptibility Testing (AST):** The antimicrobial susceptibility of identified bacterial isolates was determined using the Kirby-Bauer disk diffusion method on Mueller-Hinton agar, strictly adhering to the guidelines established by the Clinical and Laboratory Standards Institute (CLSI) (e.g., CLSI M١٠٠-ED٣٢:٢٠٢٢). Results were interpreted as Sensitive (S), Intermediate (I), or Resistant (R).

### ٢,٤ Statistical Analysis

All collected data were meticulously entered and managed using Microsoft Excel. Subsequent statistical analyses were primarily conducted using **Python programming language**, leveraging powerful libraries including Pandas for data manipulation, NumPy for numerical operations, SciPy.stats for statistical tests, and Matplotlib and Seaborn for high-quality data visualization.

#### ٢,٤,١ Descriptive Statistics

- **Continuous Variables:** For quantitative parameters (e.g., Age, Creatinine, IL levels), descriptive statistics were computed and reported as Mean ± Standard Deviation (SD). Minimum and maximum values were also presented to indicate data ranges.
- **Categorical Variables:** Frequencies and percentages were calculated for qualitative variables (e.g., Sex, Residence, Recurrent UTI, Type of bacterial infection, Antibiotic Resistance profiles).

#### ٢,٤,٢ Inferential Tests

- **Comparison of Continuous Variables Across Groups:** For comparing mean values of continuous variables among the three independent groups (Control, Hemodialysis, UTI), appropriate tests were employed. Based on distribution characteristics (visual inspection and potential formal normality tests), either **One-Way Analysis of Variance (ANOVA)** (if assumptions met) or the non-parametric **Kruskal-Wallis H-test** (if assumptions violated)

was considered. For pairwise comparisons (e.g., between recurrent vs. non-recurrent UTI patients), the **Mann-Whitney U test** was used due to its robustness.

- **Comparison of Categorical Variables:** Associations between categorical variables (e.g., Sex distribution across groups, Recurrent UTI rates) were assessed using the **Chi-square ($\chi^2$) test of independence**. **Fisher's Exact Test** was employed when expected cell counts were less than ٥.
- **Correlation Analysis:** To determine the strength and direction of linear relationships among continuous biochemical and immunological parameters within patient groups, the **Pearson correlation coefficient (r)** was calculated.

**٢,٤,٣ Data Visualization**

- **Bar charts** were utilized to graphically represent the distribution of categorical variables (e.g., sex, residence, bacterial types).
- **Box plots** were generated to visually compare the distribution and variability of continuous biochemical and immunological markers across different study groups or subgroups (e.g., recurrent vs. non-recurrent UTI).
- **Heatmaps** were employed to effectively visualize correlation matrices, illustrating the interrelationships among quantitative variables with color intensity.

A **p-value < ٠,٠٥** was consistently considered to be statistically significant for all inferential tests.

**Results**

This study presents a comprehensive statistical and descriptive analysis of three distinct cohorts: healthy controls, patients on hemodialysis, and patients diagnosed with urinary tract infections (UTIs) not undergoing dialysis therapy. All statistical analyses were performed using Python programming language, with a predetermined significance level (α) of ٠,٠٥.

## Demographic Characteristics

The demographic profiles of the participants are summarized in Tables ١, ٢, and ٣. The hemodialysis group exhibited a higher mean age (٤٨,٦٩±١٤,٦٦ years) compared to the control (٣٥,٤٩±١١,٠٣ years) and UTIs (٣٥,٨±١١,٤٨ years) groups (Table ١).

Regarding sex distribution, the control and UTIs groups showed a predominance of female participants (٥٧,١٪ and ٦٨,٦٪, respectively), while the hemodialysis group had a slight majority of male participants (٥٧,١٪) (Table ١).

For residence, both the Hemodialysis and UTIs groups had a higher proportion of participants from rural areas (٦٢,٩٪ for both), compared to the control group which showed a more balanced distribution (Table ١).

**Table ١: Age, Sex, and Residence Distribution (Frequency and Percentage)**

| **Age** | **Control Group (n=٣٥)** | **Hemodialysis Group (n=٣٥)** | **UTIs Group(n=٣٥)** |
|---|---|---|---|
| Mean | ٣٥,٤٩ | ٤٨,٦٩ | ٣٥,٨ |
| Std Dev | ١١,٠٣ | ١٤,٦٦ | ١١,٤٨ |
| **Sex** | **Control Group (n=٣٥)** | **Hemodialysis Group (n=٣٥)** | **UTIs Group (n=٣٥)** |
| Female | ٢٠ (٥٧,١٪) | ١٥ (٤٢,٩٪) | ٢٤ (٦٨,٦٪) |
| Male | ١٥ (٤٢,٩٪) | ٢٠ (٥٧,١٪) | ١١ (٣١,٤٪) |
| **Residence** | **Control Group (n=٣٥)** | **Hemodialysis Group (n=٣٥)** | **UTIs Group (n=٣٥)** |
| Rural | ١٩ (٥٤,٣٪) | ٢٢ (٦٢,٩٪) | ٢٢ (٦٢,٩٪) |
| Urban | ١٦ (٤٥,٧٪) | ١٣ (٣٧,١٪) | ١٣ (٣٧,١٪) |
| | **Control Group (n=٣٥)** | **Hemodialysis Group (n=٣٥)** | **UTIs Group (n=٣٥)** |
| Female | ٢٠ (٥٧,١٪) | ١٥ (٤٢,٩٪) | ٢٤ (٦٨,٦٪) |
| Male | ١٥ (٤٢,٩٪) | ٢٠ (٥٧,١٪) | ١١ (٣١,٤٪) |

## Biochemical Parameters

The mean and standard deviation for serum creatinine, blood urea, and fasting blood sugar levels across the three groups are presented in Tables ٤, ٥, and ٦, and visualized in Figures ٣, ٤, and ٥. The hemodialysis group showed significantly elevated mean creatinine levels (٩,٢٢±٠,٧٥ mg/dl) compared to controls (٠,٩٥±٠,١١ mg/dl) and UTIs patients (١,٠٥±٠,٠٩ mg/dl) (Table ٤).

Similarly, blood urea levels were considerably higher in the hemodialysis group (١٥٠,٩٤±٢٠,٧٥ mg/dl) than in controls (٢٩,٢٦±٦,٣٦ mg/dl) and UTIs patients (٢٨,٢٣±٧,٠٤ mg/dl) (Table ٤).

Fasting blood sugar levels were also notably higher in the hemodialysis group (١٤٣,٧١±٦٤,٢ mg/dl) compared to the control (٩٧,٨٦±١١,٥٧ mg/dl) and UTIs (٩٩,٦٣±١٣,٥٥ mg/dl) groups (Table ٤). Creatinine, blood urea, and fasting blood sugar levels in the UTIs group were comparable to the control group.

**Table ٤: Creatinine, Urea, and Fasting Blood Sugar (mg/dl) Distribution (Mean ± SD)**

| | Control Group | Hemodialysis Group | UTIs Group |
|---|---|---|---|
| Mean | ٠,٩٥ | ٩,٢٢ | ١,٠٥ |
| Std Dev | ٠,١١ | ٠,٧٥ | ٠,٠٩ |
| Mean | ٢٩,٢٦ | ١٥٠,٩٤ | ٢٨,٢٣ |
| Std Dev | ٦,٣٦ | ٢٠,٧٥ | ٧,٠٤ |
| Mean | ٩٧,٨٦ | ١٤٣,٧١ | ٩٩,٦٣ |
| Std Dev | ١١,٥٧ | ٦٤,٢ | ١٣,٥٥ |

## Immunological Marker Analysis

Table ٣ provides the mean and standard deviation for detected immunological markers. IL-٦ levels were significantly higher in both the Hemodialysis (٥٨,٨٢±١١,٢٧ pg/ml) and UTIs (٥٥,٨٦±١٤,٨٨ pg/ml) groups compared to the Control group (٢١,٧٨±١٣,٩٢ pg/ml). IL٨ levels were elevated in the Hemodialysis (٦٢,٢٨±١١,٩٣ pg/ml) and UTIs (٥٩,١٤±١٥,٧٦ pg/ml) groups, than in the Control group (٢٣,٠٦±١٤,٧٣pg/ml). Additionally, IL١٧ levels followed a similar pattern, being higher in Hemodialysis (٥٨,١٥±١٢,٨٣ pg/ml) and UTIs (٤٦,٣١±١٠,٧٩ pg/ml) groups compared to Control (٣٢,٧٦±٨,١٩ pg/ml).

**Table ٣: Immunological Markers (Mean ± SD)**

| Marker | Control Group (Mean ± SD) | Hemodialysis Group (Mean ± SD) | UTIs Group (Mean ± SD) |
|---|---|---|---|
| IL-٦ | ٢١,٧٨ ± ١٣,٩٢ | ٥٨,٨٢ ± ١١,٢٧ | ٥٥,٨٦ ± ١٤,٨٨ |
| IL-٨ | ٢٣,٠٦ ± ١٤,٧٣ | ٦٢,٢٨ ± ١١,٩٣ | ٥٩,١٤ ± ١٥,٧٦ |
| IL١٧ | ٣٢,٧٦ ± ٨,١٩ | ٥٨,١٥ ± ١٢,٨٣ | ٤٦,٣١ ± ١٠,٧٩ |

## Infection-Specific Findings

The distribution of recurrent UTIs in the Hemodialysis and UTIs groups is presented in Table ٤. All participants in the Hemodialysis group reported recurrent UTIs (١٠٠٪), while ٦٢,٩٪ of the UTIs group experienced recurrent infections.

**Table ٤: Recurrent UTI Distribution (Frequency and Percentage)**

| | Hemodialysis Group (n=٣٥) | UTIs Group (n=٣٥) |
|---|---|---|
| No | ٠ (٠,٠٪) | ١٣ (٣٧,١٪) |
| Yes | ٣٥ (١٠٠,٠٪) | ٢٢ (٦٢,٩٪) |

Table ٥ outlines the distribution of bacterial pathogens identified in both patient groups. *Escherichia coli* was the most common pathogen in both the Hemodialysis (٢٥,٧٪) and UTIs (٤٢,٩٪) groups. The Hemodialysis group also showed significant presence of *Staphylococcus aureus* (٢٠,٠٪) and *Pseudomonas aeruginosa* (١٧,١٪). The UTIs group had *Klebsiella pneumoniae* (٢٥,٧٪) and *Pseudomonas aeruginosa* (١٧,١٪) as other notable pathogens.

**Table ٥: Type of Bacterial Infection Distribution (Frequency and Percentage)**

| Type of Bacteria | Hemodialysis Group (n=٣٥) | UTIs Group (n=٣٥) |
|---|---|---|
| Escherichia coli | ٩ (٢٥,٧٪) | ١٥ (٤٢,٩٪) |
| Staphylococcus aureus | ٧ (٢٠,٠٪) | ٠ (٠,٠٪) |
| Pseudomonas aeuroginosa | ٦ (١٧,١٪) | ٠ (٠,٠٪) |
| Klebsiella pneumonia | ٥ (١٤,٣٪) | ٠ (٠,٠٪) |
| Proteus merabilus | ٣ (٨,٦٪) | ٠ (٠,٠٪) |
| Staphylococcus epidermidis | ٣ (٨,٦٪) | ٠ (٠,٠٪) |
| Acinetobacter baumannii | ٢ (٥,٧٪) | ٠ (٠,٠٪) |
| Klebsiella pneumonia | ٠ (٠,٠٪) | ٩ (٢٥,٧٪) |
| Psudomonas aeuroginosa | ٠ (٠,٠٪) | ٦ (١٧,١٪) |
| Proteus mirabillus | ٠ (٠,٠٪) | ٤ (١١,٤٪) |
| Acinetobacter baumannii | ٠ (٠,٠٪) | ١ (٢,٩٪) |

Table ٦ presents the antibiotic resistance profiles. A high rate of resistance was observed across most tested antibiotics in both groups. Ciprofloxacin showed particularly high resistance in the UTIs group (٩٤,٣٪ resistant) and also high in the Hemodialysis group (٦٨,٦٪ resistant). Gentamicin also demonstrated high resistance in both Hemodialysis (٧٧,١٪) and UTIs (٨٢,٩٪) groups.

**Table ٦: Antibiotic Resistance Profile (Frequency and Percentage)**

| Antibiotic | Resistance Type | Hemodialysis Group (n=٣٥) | UTIs Group (n=٣٥) |
|---|---|---|---|
| Amikacin | Resistant (R) | ٢٣ (٦٥,٧٪) | ٢٤ (٦٨,٦٪) |
| Amikacin | Sensitive (S) | ١٢ (٣٤,٣٪) | ١١ (٣١,٤٪) |
| Azithromycin | Resistant (R) | ١٥ (٤٢,٩٪) | ١٩ (٥٤,٣٪) |
| Azithromycin | Sensitive (S) | ٢٠ (٥٧,١٪) | ١٦ (٤٥,٧٪) |
| Levofloxacin | Resistant (R) | ٢٠ (٥٧,١٪) | ٢٩ (٨٢,٩٪) |
| Levofloxacin | Sensitive (S) | ١٥ (٤٢,٩٪) | ٦ (١٧,١٪) |
| Ciprofloxacin | Resistant (R) | ٢٤ (٦٨,٦٪) | ٣٣ (٩٤,٣٪) |
| Ciprofloxacin | Sensitive (S) | ١١ (٣١,٤٪) | ٢ (٥,٧٪) |
| Gentamicin | Resistant (R) | ٢٧ (٧٧,١٪) | ٢٩ (٨٢,٩٪) |
| Gentamicin | Sensitive (S) | ٨ (٢٢,٩٪) | ٦ (١٧,١٪) |

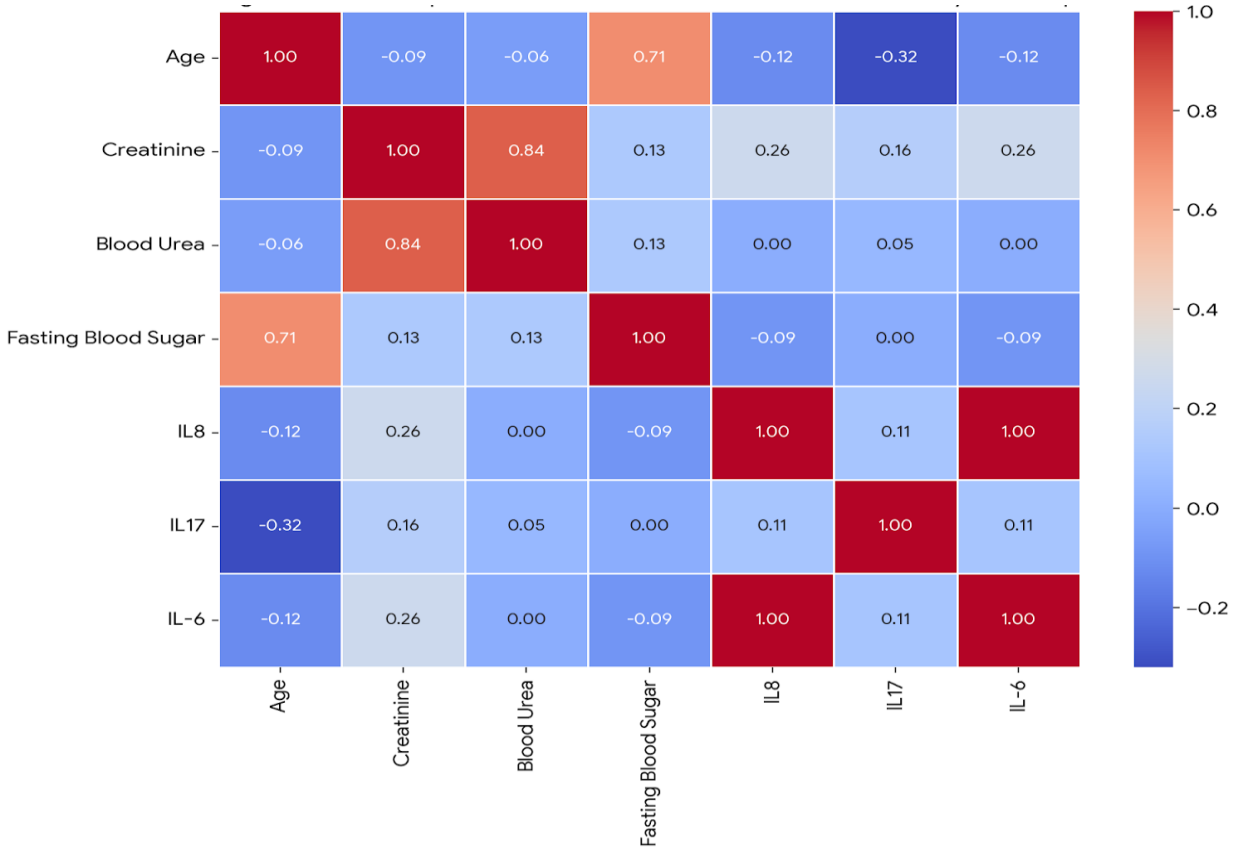
## Correlations and Associations

Table ٧ presents the Pearson correlation coefficients among quantitative variables in the Hemodialysis group. A strong positive correlation was observed between Creatinine and Blood Urea levels (r = ٠,٧٧). Moderate positive correlations were also noted between Fasting Blood Sugar and both Creatinine (r = ٠,٣٥) and Blood Urea (r = ٠,٤٣). A very strong positive correlation was observed between IL٨ and IL-٦ (r = ١,٠٠), and moderate positive correlations between these and IL١٧ (r = ٠,٣٣) (Figure ١).

**Table ٧: Pearson Correlation Matrix for Quantitative Variables in Hemodialysis Group**

| Variable | Age (year) | Creatinine (mg/dl) | Blood urea (mg/dl) | Fasting blood sugar (mg/dl) | IL٨ pg/ml | IL١٧ pg/ml | IL-٦ pg/ml |
|---|---|---|---|---|---|---|---|
| **Age (year)** | ١,٠٠ | ٠,٠٥ | -٠,١٦ | ٠,٠٨ | -٠,١٧ | -٠,٠٦ | -٠,١٧ |
| **Creatinine (mg/dl)** | ٠,٠٥ | ١,٠٠ | ٠,٧٧ | ٠,٣٥ | -٠,٠٥ | ٠,٠٣ | -٠,٠٥ |
| **Blood urea (mg/dl)** | -٠,١٦ | ٠,٧٧ | ١,٠٠ | ٠,٤٣ | ٠,١٢ | ٠,٠٧ | ٠,١٢ |
| **Fasting blood sugar (mg/dl)** | ٠,٠٨ | ٠,٣٥ | ٠,٤٣ | ١,٠٠ | -٠,١٤ | ٠,٠٣ | -٠,١٤ |
| **IL٨ pg/ml** | -٠,١٧ | -٠,٠٥ | ٠,١٢ | -٠,١٤ | ١,٠٠ | ٠,٣٣ | ١,٠٠ |
| **IL١٧ pg/ml** | -٠,٠٦ | ٠,٠٣ | ٠,٠٧ | ٠,٠٣ | ٠,٣٣ | ١,٠٠ | ٠,٣٣ |
| **IL-٦ pg/ml** | -٠,١٧ | -٠,٠٥ | ٠,١٢ | -٠,١٤ | ١,٠٠ | ٠,٣٣ | ١,٠٠ |

**Figure ١: Heatmap of Pearson Correlation Matrix for Hemodialysis Group**




For the UTIs group, Table ٨ and Figure ٢ show generally weak linear relationships among demographic, biochemical, and immunological markers. A strong positive correlation was noted between IL-٨ and IL-٦ (r = ١,٠٠), and a moderate positive correlation between IL-٨ and IL-١٧ (r = ٠,٣٢), as well as IL-٦ and IL-١٧ (r = ٠,٣٢)

**Table ٨: Pearson Correlation Matrix for Quantitative Variables in UTIs Group**

| | Age | Creatinine | Blood Urea | Fasting Blood Sugar | IL٨ | IL١٧ | IL-٦ |
|---|---|---|---|---|---|---|---|
| Age | ١,٠٠ | ٠,٠٣ | ٠,٠٣ | ٠,٠٥ | -٠,٢٤ | ٠,٢٢ | -٠,٢٤ |
| Creatinine | ٠,٠٣ | ١,٠٠ | -٠,١٨ | ٠,٠٥ | -٠,١٣ | -٠,٢٠ | -٠,١٣ |
| Blood Urea | ٠,٠٣ | -٠,١٨ | ١,٠٠ | -٠,٢٣ | ٠,١٠ | ٠,٢٠ | ٠,١٠ |
| Fasting Blood Sugar | ٠,٠٥ | ٠,٠٥ | -٠,٢٣ | ١,٠٠ | -٠,٠٢ | -٠,٣١ | -٠,٠٢ |
| IL٨ | -٠,٢٤ | -٠,١٣ | ٠,١٠ | -٠,٠٢ | ١,٠٠ | ٠,٣٢ | ١,٠٠ |
| IL١٧ | ٠,٢٢ | -٠,٢٠ | ٠,٢٠ | -٠,٣١ | ٠,٣٢ | ١,٠٠ | ٠,٣٢ |
| IL-٦ | -٠,٢٤ | -٠,١٣ | ٠,١٠ | -٠,٠٢ | ١,٠٠ | ٠,٣٢ | ١,٠٠ |

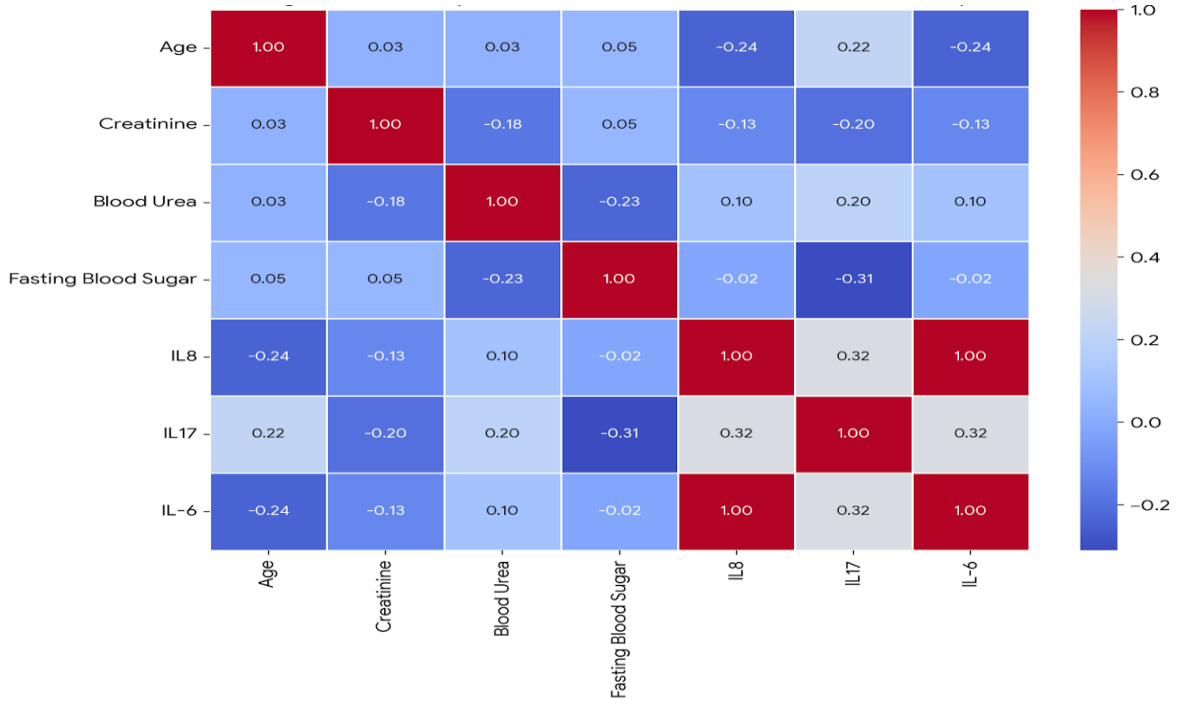



**Figure ٢: Heatmap of Pearson Correlation Matrix for UTIs Group**

Table ٩ presents the comparison of quantitative variables by recurrent UTI status in the UTIs group. The Mann-Whitney U test results indicate no statistically significant differences (p>٠,٠٥) between patients with and without recurrent UTIs for any of the tested quantitative variables.

**Table ٩: Comparison of Quantitative Variables by Recurrent UTI Status in UTIs Group**

| Variable | Recurrent UTI: Yes (Mean ± SD) | Recurrent UTI: No (Mean ± SD) | p-value (Mann-Whitney U) |
|---|---|---|---|
| Age | ٣٧,٤٥ ± ١٢,٢٠ | ٣٣,٠٠ ± ٩,٩٧ | ٠,٢٦٠ |
| Creatinine | ١,٠٦ ± ٠,٠٩ | ١,٠٣ ± ٠,١٠ | ٠,٥٠٥ |
| Blood Urea | ٢٧,٣٦ ± ٧,١٧ | ٢٩,٦٩ ± ٦,٨٢ | ٠,٣٤٧ |
| Fasting Blood Sugar | ١٠٢,٣٢ ± ١٣,٧٥ | ٩٥,٠٨ ± ١٢,٤١ | ٠,١٣٧ |
| IL-٨ | ٥٧,١٧ ± ١٨,٢٢ | ٦٣,٠٨ ± ٨,٥٦ | ٠,٥٢٣ |
| IL-١٧ | ٤٤,١٧ ± ٩,٨٨ | ٥٠,٥٩ ± ١١,٧٦ | ٠,١٥٣ |
| IL-٦ | ٥٤,٠٠ ± ١٧,٢١ | ٥٩,٥٧ ± ٨,٠٩ | ٠,٥٢٣ |

## Discussion

This study aimed to provide a comprehensive comparative analysis of demographic, biochemical, immunological, and microbiological profiles, including antimicrobial resistance patterns, among healthy controls, hemodialysis patients, and non-dialysis patients with confirmed urinary tract infections (UTIs). Our findings reveal distinct characteristics across these cohorts, underscoring the complex interplay of underlying conditions, host immune responses, and infectious challenges.

**Demographic and Clinical Context:** The demographic analysis revealed an older mean age in the hemodialysis group compared to both controls and UTI patients. This aligns with the epidemiology of end-stage renal disease (ESRD), where age is a significant risk factor for kidney dysfunction [١،٢]. The male predominance in the hemodialysis cohort, contrasted with the female majority in the UTI group, is consistent with known epidemiological trends: UTIs are more prevalent in younger females due to anatomical and physiological factors [٣،٦], while male predominance in ESRD can be multifactorial, potentially linked to underlying causes like hypertension or glomerulonephritis, or differences in healthcare access [٨]. The higher representation of rural residents in both patient groups suggests potential disparities in early healthcare access or chronic disease management in these regions, which might contribute to advanced disease states requiring dialysis or recurring infections [٩]. The universal prevalence of recurrent UTIs in the hemodialysis group (١٠٠٪) highlights their profound vulnerability to repeat infections, largely attributed to their immunocompromised state,frequent hospitalizations, and indwelling catheter use [٥،١١]. While recurrent UTIs were also common in the non-dialysis UTI group, their underlying risk factors are likely distinct, emphasizing the need for tailored preventive strategies [٢٨].

**Biochemical and Metabolic Status:** As anticipated, hemodialysis patients demonstrated significantly elevated serum creatinine and blood urea levels. These markers are direct indicators of impaired renal function and uremic toxin accumulation, which are hallmarks of ESRD [١٤,١٥]. The markedly higher fasting blood sugar levels in the hemodialysis group further underscore the high prevalence of diabetes mellitus or significant insulin resistance within this population, a major comorbidity and a leading cause of ESRD globally [٣,١٦]. These biochemical derangements not only reflect the severity of renal disease but also contribute to the overall physiological stress and altered host defense mechanisms, increasing susceptibility to infections [٤,١٧]. In contrast, the UTI group's biochemical profiles were largely comparable to the control group, suggesting that their UTIs were generally community-acquired and not typically associated with severe acute kidney injury or chronic metabolic dysregulation that would significantly alter these systemic markers.

**Immunological Landscape:** A pivotal finding of this study is the elevated inflammatory cytokine profiles in both patient groups compared to controls. Both hemodialysis and UTI groups exhibited significantly higher mean levels of IL-٦ and IL١٧. IL-٦ is a pleiotropic cytokine central to systemic inflammation and acute-phase responses, often elevated in chronic inflammatory conditions like ESRD and acute infections [٢٠,٢١]. Its elevated levels in hemodialysis patients reflect the chronic inflammatory state ("malnutrition-inflammation complex syndrome") commonly seen in dialysis patients [٢,٢٠,٢١]. In UTIs, IL-٦ elevation indicates an active immune response to bacterial invasion [٢٢]. IL١٧, a key cytokine in Th١٧-mediated immunity, is involved in host defense against extracellular bacteria and fungi but also contributes to chronic inflammation [٢٠]. Its elevated levels in both patient groups suggest its role in the immune response to infection and underlying inflammatory processes. Similarly, elevated IL-٨ in both patient groups in

comparison to control group to signifies active neutrophil chemotaxis and acute inflammatory responses to bacterial pathogens [٢٠,٢١]. These findings underscore a significant immune dysregulation in both patient cohorts, albeit possibly via different primary pathways, contributing to their susceptibility and response to infection.

**Microbiological Patterns and Antimicrobial Resistance:** *Escherichia coli* remains the most prevalent uropathogen in both hemodialysis and non-dialysis UTI patients, consistent with global epidemiological data for both community-acquired and healthcare-associated UTIs [١٣,٢٤]. However, the hemodialysis group showed a greater diversity of isolated pathogens, including *Staphylococcus aureus* and *Pseudomonas aeruginosa*. These organisms are frequently associated with healthcare-associated infections, device-related infections, and complications in immunocompromised individuals [١٤,١٥]. This higher microbial diversity in hemodialysis patients is likely a direct consequence of their frequent contact with healthcare settings and repeated antibiotic exposure, leading to the selection of more resistant and opportunistic pathogens [١٦,١٧]. The observed high rates of antibiotic resistance, particularly to Ciprofloxacin and Gentamicin, across both patient groups, but more pronounced in the UTI group for Ciprofloxacin, are alarming. This finding highlights the escalating challenge of antimicrobial resistance and underscores the need for robust antimicrobial stewardship programs. The high resistance in hemodialysis patients is particularly concerning given their limited treatment options and increased risk of morbidity and mortality from resistant infections [١٠]. The higher resistance rates in the UTI group for some agents like Ciprofloxacin suggest the spread of highly resistant community-acquired strains, or the impact of prior antibiotic exposure.

**Correlations and Associations:** The strong positive correlations between creatinine and blood urea levels in both patient groups are a physiological constant, reflecting the close relationship of these markers in assessing renal function [١٨,١٩].The distinct patterns of correlation for immunological markers (e.g., IL-٦, IL٨, IL١٧) within each patient group indicate their complex interactions in disease-specific inflammatory responses. While this study did not find statistically significant associations between age, biochemical markers, or immunological markers and recurrent UTI status within the non-dialysis UTI group, this might be influenced by the sample size or the multifactorial nature of UTI recurrence, which could involve genetic, anatomical, or behavioral factors not measured in this study [٢٨]. Future larger studies or those incorporating a wider range of potential risk factors are warranted to further explore these associations.

**Limitations and Future Directions:** This study's cross-sectional design limits our ability to establish causality or observe disease progression over time. The sample size, while sufficient for initial comparisons, may have limited the power to detect subtle associations or significant differences in certain subgroups. Future research should consider longitudinal designs, larger and more diverse patient cohorts, and expand the panel of immunological markers and other host response indicators. Comprehensive genomic and resistome profiling of bacterial isolates could also provide deeper insights into the mechanisms of antimicrobial resistance and pathogen transmission within these vulnerable populations.

## Conclusion

This study offers an in-depth comparative analysis of demographic, biochemical, immunological, and microbiological profiles across healthy controls, hemodialysis patients, and non-dialysis patients with urinary tract infections. The findings unequivocally demonstrate that hemodialysis patients present a distinct and complex clinical and laboratory profile characterized by profound biochemical derangements indicative of ESRD, a heightened systemic inflammatory state evidenced by elevated IL-٦, IL-٨, and IL-١٧ levels, and a broader spectrum of bacterial infections with alarming rates of antimicrobial resistance. While *Escherichia coli* remains the primary uropathogen, the increased diversity of bacterial species and widespread resistance in hemodialysis patients, contrasted with the non-dialysis UTI cohort, highlights the unique challenges in managing infections in this vulnerable population. These results underscore the critical necessity for differentiated diagnostic, therapeutic, and preventive approaches, including robust infection control measures and targeted antimicrobial stewardship programs, specifically tailored for hemodialysis units and patients. Future research should focus on longitudinal designs, larger cohorts, and advanced immunological and microbiological investigations to further elucidate host-pathogen interactions and improve patient outcomes.

## References


١. **Yamashita, K., Ishiyama, Y., Yoshino, M., Tachibana, H., Toki, D., & Kondo, T. (٢٠٢٢). Urinary tract infection in hemodialysis-dependent end-stage renal disease patients. *Research and Reports in Urology*, ١٤, ٧–١٥.**

٢. **Kalantar-Zadeh, K., Ikizler, T. A., Block, G., Avram, M. M., & Kopple, J. D. (٢٠٠٣). Malnutrition-inflammation complex syndrome in dialysis patients: causes and consequences. *American Journal of Kidney Diseases*, ٤٢(٥), ٨٦٤–٨٨١.**

٣. **Golebiewska, J. E., Debska-Slizien, A., & Rutkowski, B. (٢٠٢١). Urinary tract infections in patients with renal insufficiency and dialysis. *GMS Infectious Diseases*, ٩, Doc٠٧.**

٤. **Avram, M. M., Goldwasser, P., Erroa, M., & Fein, P. A. (١٩٩٤). Predictors of survival in continuous ambulatory peritoneal dialysis patients. *American Journal of Kidney Diseases*, ٢٣(١), ٩١–٩٨.**

٥. **Singh, R., Devi, S., & Singh, S. (٢٠١٦). Frequency of urinary tract bacterial infection and their susceptibility patterns among hemodialysis patients in Zliten Hospital. *Journal of Microbiology and Experimentation*, ٣(١), ١–٥.**

٦. **Oikonomou, K., & Alhaddad, A. (٢٠١٦). Diagnostic value of urinalysis in hemodialysis patients with fever or suspected UTI. *Journal of Clinical and Diagnostic Research*, ١٠(١٠), OC١١–OC١٣.**

٧. **Kundu, R., & Das, S. (٢٠١٩). Microbiological profile of urinary tract infection in patients with burn injuries. *International Journal of Research in Medical Sciences*, ٧(٨), ٢٨٩٢–٢٨٩٦.**

٨. **Prabhu, A., & Oommen, S. (٢٠١٧). Clinico-microbiological profile of urinary tract infections in a tertiary care hospital. *Journal of Clinical and Diagnostic Research*, ١١(٦), DC٠١–DC٠٣.**

٩. **Vij, M., & Nataraj, G. (٢٠٠٩). Diagnostic utility of urinalysis in detecting urinary tract infection in hemodialysis patients. *Nephron Clinical Practice*, ١١٣(٤), c٢٨١–c٢٨٧.**

١٠. **Jaiswal, S., Sharma, R., & Paudel, P. (٢٠١٣). Bacteriological study of UTI in male dialysis patients with chronic kidney disease. *International Journal of Health Sciences Research*, ٣(٥), ١–٥.**

١١. Haritham, V., & Rahman, S. (٢٠٢١). Microbiological profile of UTIs in males: A cross-sectional study. *International Journal of Research in Medical Sciences*, ٩(٣), ٧٨٩–٧٩٣.

١٢. Bajpai, S., Kumar, D., & Chaturvedi, T. (٢٠١٨). Clinical and microbiological profile of UTIs in children and antibiotic resistance pattern. *International Journal of Contemporary Medical Research*, ٥(١١), K١–K٥.

١٣. Hegazy, M. E., El-Hamid, R. A., El-Din, A. E., et al. (٢٠١٨). Microbiological profile of UTIs with special reference to E. coli. *International Journal of Current Microbiology and Applied Sciences*, ٧(٢), ١١٥–١٢٥.

١٤. Fabian, F. S. P., Cremades, R., Pinto, E. S. A., et al. (٢٠٢٣). Microbiological profile of UTIs in a Western Mexico tertiary hospital. *Scientific Progress*, ١٠٦(١), ١–١١.

١٥. Kireports Study Group. (٢٠٢٤). Clinical and microbiological profile of UTIs in febrile children in India. *Kidney International Reports*, ٩(٣), S٢٤٦٨–S٠٢٤٩.

١٦. Treacy, O. (٢٠١٨). Biochemical evaluation of kidney disease. *Translational Andrology and Urology*, ٧(٤), ٥٩٤–٦٠٥.

١٧. Tomayko, E. J., Kistler, B. M., Fitschen, P. J., et al. (٢٠١٥). Protein supplementation during dialysis reduces inflammation. *Journal of Renal Nutrition*, ٢٥(٥), ٤٥٧–٤٦٥.

١٨. Lambert, K., Lightfoot, C. J., Jegatheesan, D. K., et al. (٢٠٢٢). Physical activity recommendations for dialysis patients. *PLOS ONE*, ١٧(٤), e٠٢٦٧٠٤٢.

١٩. Yamada, S., Arase, H., Yoshida, H., et al. (٢٠٢٢). Malnutrition-Inflammation Complex Syndrome in hemodialysis: Q-Cohort Study. *Scientific Reports*, ١٢(١), ١–١٠.

٢٠. Kalantar-Zadeh, K., Kopple, J. D., Block, G., & Humphreys, M. H. (٢٠٠١). Malnutrition-inflammation score and morbidity in dialysis. *American Journal of Kidney Diseases*, ٣٨(٦), ١٢٥١–١٢٦٣.

٢١. Kanda, E., Lopes, M. B., Tsuruya, K., et al. (٢٠٢١). Malnutrition-inflammation and functional limitations in hemodialysis. *Scientific Reports*, ١١(١), ١–١٠.

٢٢. Jitendranath, R., & Radhika, R. (٢٠١٦). Microbiological profile of UTIs in pediatric populations. *Journal of Clinical and Diagnostic Research*, ١٠(٩), DC١٧–DC١٩.

٢٣. Medscape Editors. (٢٠٢٢). Novel biomarkers of kidney function: Overview. Retrieved from https://emedicine.medscape.com

٢٤. FastMed Clinics. (٢٠٢٢). Urinary Tract Infections (UTIs): Causes and treatment. Retrieved from https://www.fastmed.com

٢٥. Rao, T. V. (٢٠١٦). Infections in dialysis patients: Basis and prevention. Retrieved from https://www.scribd.com

٢٦. Golebiewska, J. E., Debska-Slizien, A., & Rutkowski, B. (٢٠٢١). UTI risk and management in dialysis. *GMS Infectious Diseases*, ٩, Doc٠٧.

٢٧. Alp Ikizler, T. A., & Kovesdy, C. P. (٢٠١٤). Nutrition and inflammation in CKD. *Current Opinion in Nephrology and Hypertension*, ٢٣(٤), ٣٠٣–٣١٠.

٢٨. Erek, E., Sever, M. S., & Ataman, R. (٢٠٠٠). Dialysis and infection risks in developing countries. *Kidney International*, ٥٧, S١١١–S١١٤.

٢٩. World Health Organization. (٢٠٢١). Antimicrobial resistance in healthcare-associated infections. Retrieved from https://www.who.int

٣٠. Zoccali, C., Torino, C., Tripepi, G., et al. (٢٠١٧). Biomarkers and risk stratification in CKD. *Nature Reviews Nephrology*, ١٣(١٠), ٥٧٦–٥٨٥.