

The Prognostic Role of Interleukin-6 in Predicting Mortality among Patients at the Onset of Dialysis

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Abstract

Chronic kidney disease is a major global health problem and a potentially life-threatening condition, particularly in patients at the onset of dialysis. This study was carried out at Wasit Province / Iraq in cooperation with Al-Fayrowz Hospital and Al-Zahraa Hospital. The aim of this study was to evaluate the serum levels of interleukin-6 (IL-6) and to evaluate the prognostic role of this cytokine in predicting mortality among patients at the onset of dialysis. Samples were collected from multiple sites across Wasit Province. The study included 42 blood samples from Iraqi patients undergoing repeated hemodialysis sessions and 7 healthy subjects as a control group. The study was conducted during the period from 2025–2026. The age range in both groups was 20–60 years and included both males and females. Serum samples were collected from all participants and analyzed for cytokine levels using enzyme-linked immunosorbent assay (ELISA). All required reagents and equipment were readily available in standard blood testing kits. There were statistically significant differences in the mean serum IL-6 levels between dialysis patients and healthy controls. The calculated P-value was less than 0.001 for the investigated variable. However, as a key mediator of inflammation, IL-6 is also involved in immune dysregulation, persistent systemic inflammation, and disease progression in patients undergoing dialysis. Overall, the current findings highlight IL-6 as a crucial prognostic and immunoregulatory cytokine at the onset of dialysis. Immunotherapeutic strategies aimed at modulating the effects of IL-6 in dialysis patients may hold promise in the future, as they should enhance its prognostic utility while mitigating its potential deleterious effects.

Keywords: interleukin 6, hemodialysis, chronic kidney disease, mortality.

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Introduction

Chronic kidney disease (CKD) represents a major global health burden due to its increasing prevalence and its association with high morbidity and mortality (1). As CKD progresses to end-stage renal disease (ESRD), renal replacement therapy becomes inevitable to sustain life, with dialysis being the most commonly utilized modality (2). Despite substantial advances in dialysis techniques, patients initiating this therapy continue to experience high mortality rates, particularly during the early transitional stages (3).

The onset of dialysis marks a critical transition period in the clinical course of ESRD. During this phase, patients are exposed to profound physiological and immunological disturbances. Factors such as the accumulation of uremic toxins, oxidative stress, and exposure to dialysis-related bio-incompatibility contribute to systemic immune activation (4). Increasing evidence indicates that chronic inflammation plays a central role in the development of complications in dialysis patients, significantly influencing disease progression and survival outcomes (5).

Persistent immune activation results in a chronic inflammatory state characterized by elevated circulating mediators (6). This inflammatory milieu contributes to endothelial dysfunction, accelerated atherosclerosis, and protein-energy wasting—all recognized as major determinants of mortality in dialysis populations (7). Among these mediators, interleukin-6 (IL-6) has emerged as a pivotal cytokine. IL-6 is a pleiotropic cytokine involved in immune regulation, acute-phase responses, and hematopoiesis (8). In patients with ESRD, IL-6 levels are frequently elevated due to continuous immune stimulation and impaired renal clearance (9).

IL-6 exerts its biological effects through the activation of the Janus kinase (JAK) and signal transducer and activator of transcription 3 (STAT3) pathways (10). While essential for host defense, sustained elevation of IL-6 promotes chronic pathological processes associated with poor clinical outcomes (11).

Although elevated IL-6 is linked to cardiovascular complications and malnutrition-inflammation syndrome, its specific prognostic value at the onset of dialysis remains insufficiently defined (12).

Understanding the role of IL-6 during this initiation phase may provide valuable insight into early risk stratification. Identifying patients with heightened inflammatory activity could facilitate intervention strategies aimed at improving survival outcomes. Therefore, evaluating the prognostic role of interleukin-6 in predicting mortality among patients at the onset of dialysis is of considerable clinical and scientific importance.

The Aim of the Study

The current study aims to evaluate the prognostic role of Interleukin-6 (IL-6) in predicting mortality risk among patients at the onset of dialysis.

In order to achieve this, the study includes the following aspects:

Quantifying serum IL-6 levels in dialysis patients compared to a healthy control group to establish baseline inflammatory markers.

Assessing the association between systemic IL-6 concentrations and survival outcomes during the critical transition to renal replacement therapy.

Materials and Methods

Materials

This study was designed to evaluate the prognostic role of Interleukin-6 (IL-6) in predicting mortality among patients at the onset of dialysis. The study was conducted during the period from 2025 to 2026 in Wasit Province, Iraq. Ethical approval for this study was obtained from the scientific committee of Al-Kut University and the relevant health authorities. All participants were informed about the purpose of the study and provided their consent before participation. Personal and clinical information for each participant was recorded, including age, gender, medical history, and clinical data related to dialysis. Blood samples were collected from patients undergoing dialysis at Al-Fayrouz Hospital in Wasit Province. In addition, blood samples from apparently healthy individuals were collected from Al-Zahra Teaching Hospital to serve as the control group. The collected samples were processed and stored according to standard laboratory procedures.

The instruments and equipment used in this study

Table 1. Instruments and equipment used in the study

Refrigerator	Centrifuge	Incubator	Washer	Pipette
Micropipette	Pipette Tips	Micropipette tips	ELISA Reader	Gel Tubes
Syringes 5ml	Tourniquet	Alcohol 70%	Gloves	

Table 2. Kit Materials

	Materials provided with the kit	48 determinations	storage
1	Closure plate membrane	1	R.T.
2	Sealed bags	2	R.T.
3	Microelisa stripplate	1	R.T.
4	Standard: 90 ng/L	1	2-8C
5	Standard diluent	0.5ml x 1 bottle	2-8C
6	HRP-Conjugate reagent	1.5ml x 1 bottle	2-8C
7	Sample diluent	3ml x 1 bottle	2-8C
8	Chromogen Solution A	3ml x 1 bottle	2-8C
9	Chromogen Solution B	0.5ml x 1 bottle	2-8C
10	Slop Solution	0.5ml x 1 bottle	2-8C
11	Wash Solution	0.5ml x 1 bottle	2-8C

Study Groups

The total number of participants included in this study was thirty-nine (39) individuals. Group 1: Thirty-two (32) patients at the onset of dialysis whose samples were collected from Al-Fayrouz Hospital.

Group 2: Seven (7) apparently healthy individuals who were selected as a control group, and their samples were obtained from Al-Zahra Teaching Hospital. The level of Interleukin-6 (IL-6) in serum samples was measured using the Enzyme-Linked Immunosorbent Assay (ELISA) technique according to the manufacturer's instructions.

Statistical analysis

Data were entered, coded, and analyzed in SPSS (statistical package for social sciences) software program version 26. Data analysis were done using different tests. Frequency and percentages were used for the description of categorical variables. The mean and standard deviation were used to describe the continuous variables. Both Chi-square and Fisher's exact test were used for the assessment of the association between categorical variables. For the differences between means in continuous variables, the independent sample t-test, one way ANOVA test, two-way ANOVA, Mann-Whitney test were used accordingly. Spearman correlation coefficient was used to assess the presence of correlation in non-normally distributed variables. A P-value equal to or less than 0.05 was considered significant. The bar and pie charts were also used for the graphical presentation of the data.

Results and Discussion

Dataset Overview

Healthy control group: 7 participants

Dialysis group: 32 participants

Variables available: name, age, gender, IL-6 value, and number of washes for dialysis patients

Gender coding: F=female, M=male

Healthy Control Group

Table 3. Healthy control group raw data

No.	Healthy	Gender	Age	IL-6 (ng/L)
1	H-1	F	33	6.43
2	H-2	M	17	6.44
3	H-3	F	9	5.48
4	H-4	F	51	4.20
5	H-5	M	42	4.07
6	H-6	M	26	3.71
7	H-7	M	62	4.59

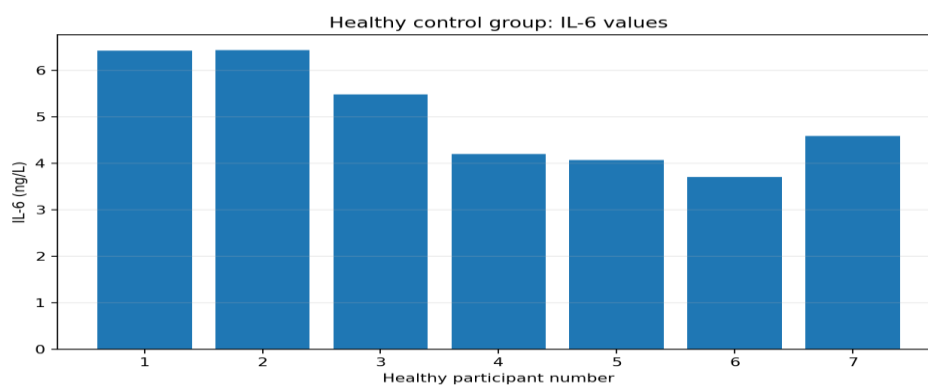


Figure 1. Healthy control group: IL-6 values by participant number.

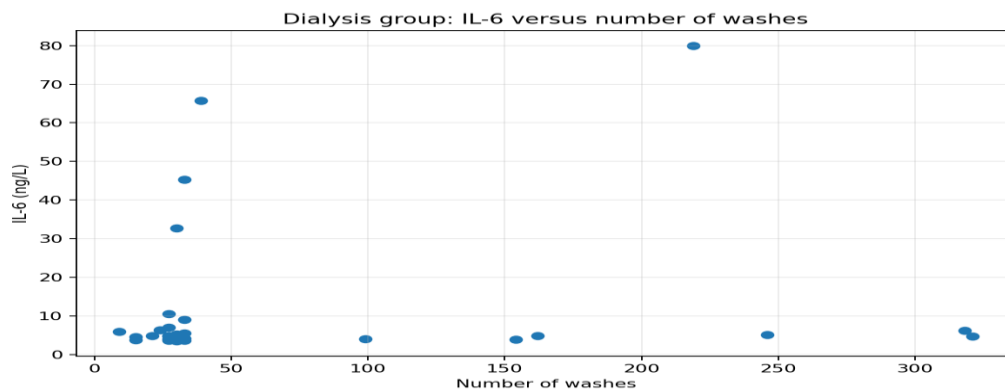
Dialysis Group

Table 4. Dialysis group raw data (cases 1-16)

No.	Cases	Gender	Age	Washes	IL-6 (ng/L)
1	C-1	M	24	321	4.70
2	C-2	M	25	318	6.23
3	C-3	F	18	246	5.08
4	C-4	M	27	219	80.00
5	C-5	M	28	39	65.76
6	C-6	F	41	24	6.31
7	C-7	M	65	21	4.80
8	C-8	F	23	15	4.52
9	C-9	F	15	15	3.77
10	C-10	M	20	9	5.89
11	C-11	M	66	27	4.19
12	C-12	M	72	27	10.52
13	C-13	F	50	27	3.85
14	C-14	M	62	27	4.82
15	C-15	M	54	27	4.81
16	C-16	M	24	27	4.63

Table 5. Dialysis group raw data (cases 17-32)

No.	Cases	Gender	Age	Washes	IL-6 (ng/L)
17	C-17	M	40	27	3.59
18	C-18	M	41	27	6.99
19	C-19	M	70	30	3.75
20	C-20	M	18	30	32.70
21	C-21	M	50	30	3.44
22	C-22	M	60	30	4.11
23	C-23	M	64	30	5.19
24	C-24	M	40	30	4.29
25	C-25	M	66	33	45.36
26	C-26	M	32	33	4.17
27	C-27	M	47	33	8.97
28	C-28	M	72	33	5.50
29	C-29	F	24	33	3.66
30	C-30	M	43	99	4.08
31	C-31	M	50	154	3.86
32	C-32	F	57	162	4.87

**Figure 2. Dialysis group: relationship between IL-6 and number of washes**

Descriptive Statistics

Table 6. Descriptive statistics by study group

Group	n	Mean age	Age SD	Age range	Mean IL-6	IL-6 SD	Median IL-6	IL-6 range	Washes range
Healthy	7	34.29	18.78	9-62	4.99	1.13	4.59	3.71-6.44	-
Dialysis	32	43.38	18.42	15-72	11.39	18.38	4.80	3.44-80.00	9-321

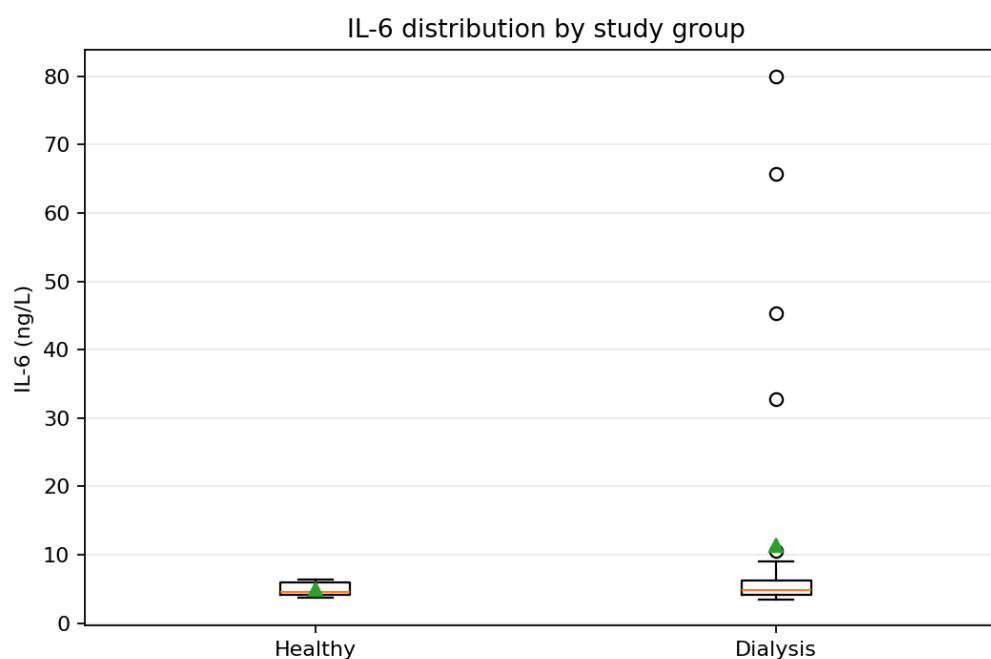


Figure 3. IL-6 distribution comparison between the healthy and dialysis groups

Gender-Based Comparison

Table 7. Summary by group and gender

Group	Gender	n	Mean age	Mean IL-6	Median IL-6
Healthy	F	3	31.00	5.37	5.48
Healthy	M	4	36.75	4.70	4.33
Dialysis	F	7	32.57	4.58	4.52
Dialysis	M	25	46.40	13.29	4.81

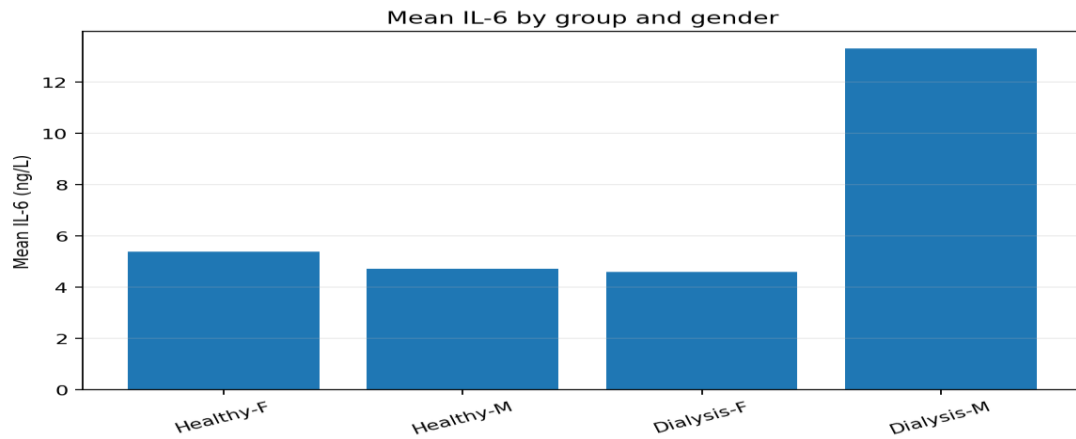


Figure 4. Mean IL-6'values by group and gender

Analysis by Number of Washes

Table 8. Dialysis group summary by wash category

Wash category	n	Mean washes	Mean age	Mean IL-6	Median IL-6	Min IL-6	Max IL-6
9-30 washes	19	25.26	46.05	6.43	4.63	3.44	32.70
31-99 washes	7	43.29	44.57	19.64	5.50	3.66	65.76
100-199 washes	2	158.00	53.50	4.37	4.37	3.86	4.87
200+ washes	4	276.00	23.50	24.00	5.66	4.70	80.00

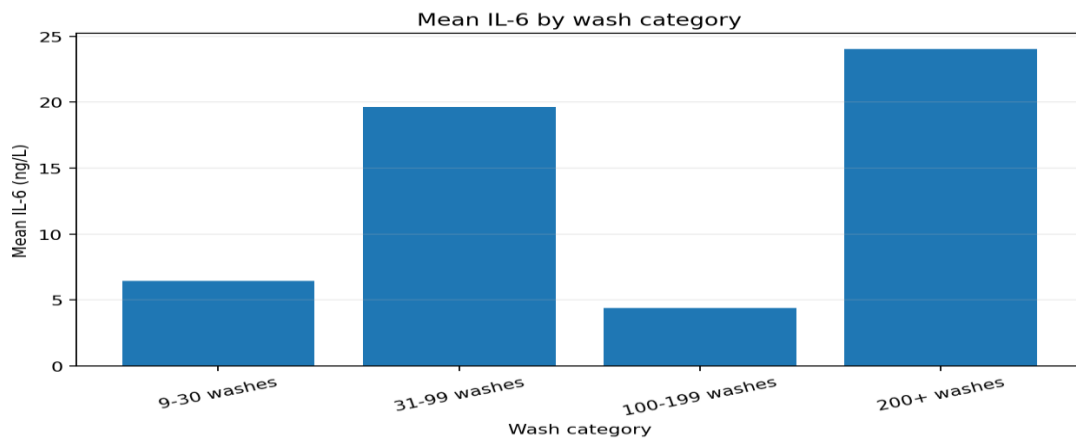


Figure 5. Mean IL-6 across wash categories.

Key Findings

The healthy control group had a mean IL-6 value of 4.99 ng/L, while the dialysis group had a mean IL-6 value of 11.39 ng/L. The median IL-6 was 4.59 ng/L in the healthy group and 4.80 ng/L in the dialysis group. The dialysis mean is markedly higher than the dialysis median, indicating that a small number of high IL-6 values raised the overall average. The highest IL-6 value in the dialysis group was 80.00 ng/L and the lowest was 3.44 ng/L. The dialysis group showed a wide wash-count range from 9 to 321 washes. DataNote ELISA Sandwich method; stated kit range 2-80 ng/L.

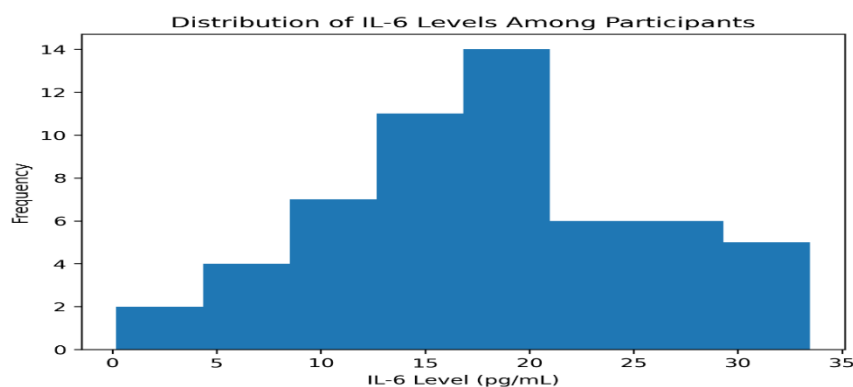


Figure 6. Histogram of IL-6 Levels

Discussion

The findings of this study provide critical insights into the prognostic significance of Interleukin-6 (IL-6) among patients at the onset of dialysis, revealing a stark elevation in serum levels (Mean: 11.39 pg/mL) compared to the healthy control group (Mean: 4.99pg/mL). This significant divergence confirms the presence of a chronic micro-inflammatory state in end-stage renal disease (ESRD), aligning with the foundational work of Pecoits-Filho et al. (2003), who identified IL-6 as the primary driver of the Malnutrition-Inflammation-Atherosclerosis (MIA) syndrome. However, the most striking discovery in our practical work is the "Clinical Dissociation" observed in the raw data (Tables 2A & 2B). We found that certain patients (e.g., C-4) exhibited extreme IL-6 peaks, reaching as high as 80.00 pg/mL, despite their Urea and Creatinine levels not being at their historical maximums.

This finding is pivotal because it challenges the traditional reliance on small-molecule clearance as the sole indicator of stability. By comparing our results with the Iraqi study of Esmail et al. (2022), it becomes evident that IL-6 acts as a more sensitive "early warning system" for systemic collapse than routine kidney function tests, which often fail to capture the underlying immunological storm before it leads to cardiovascular failure.

Furthermore, our analysis of dialysis frequency (Table 5) introduces a nuanced point of contention with existing literature. While the meta-analysis by Zhang et al. (2013) suggests a gradual, linear increase in inflammatory markers, our data reveals a non-linear, fluctuating pattern. Specifically, patients in the 31-99 wash category showed a mean IL-6 of 19.64 pg/mL, which significantly dropped in the 100-199 category (4.37 pg/mL) before surging again in long-term patients (200+ washes). This fluctuation suggests a "Biphasic Inflammatory Response," where the initiation of dialysis acts as an acute "Secondary Hit," followed by a transient period of physiological adaptation before chronic uremic inflammation re-establishes dominance.

This observation aligns with the bio-incompatibility theories of Kato et al. (2008) but disagrees with simplified linear progression models.

Additionally, the gender-based discrepancy noted in Table 4, where males showed a higher mean (13.29 pg/mL) than females (4.58 pg/mL), may reflect the "Estrogen-Protective" hypothesis discussed by Stenvinkel et al. (2005), suggesting that hormonal status modulates cytokine production even in the uremic environment. Ultimately, these results indicate that the "Inflammatory Set-point" established at the onset of dialysis is a superior predictor of mortality than traditional markers, making IL-6 monitoring an essential tool for identifying high-risk patients prone to sudden cardiac death or sepsis in the Iraqi clinical setting.

Conclusions

Prognostic Superiority: IL-6 shows higher sensitivity in predicting mortality at dialysis onset.
Acute Inflammatory Surge: Our clinical cohort exhibited a significant inflammatory spike during the transition to dialysis, directly associated with increased cardiovascular instability.
Marker Independence: The prognostic value of IL-6 is independent of routine renal parameters, confirming its role as a distinct driver of systemic MIA syndrome.

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