Al-Azhar International Medical Journal

Volume 5 | Issue 1 Article 16

2024
Section: Internal Medicine

Effect of Low-Flux versus High-Flux Dialyzers on Interleukin 6 (IL-6) Level in Patients Undergoing Maintenance Haemodialysis

Hussein Salem Farahat Salem
Department of Internal Medicine, Faculty of Medicine, Al- Azhar University, Hussein.farahat80@gmail.com

Mohamed Nabil Raafat
Department of Internal Medicine, Faculty of Medicine, Al- Azhar University

Ismail Mohamed El Mancy
Department of Internal Medicine, Faculty of Medicine, Al- Azhar University

Ibrahim Metwaly Bayomi
Department of Clinical Pathology, Faculty of Medicine, Al- Azhar University

How to Cite This Article

Salem, Hussein Salem Farahat; Raafat, Mohamed Nabil; Mancy, Ismail Mohamed El; and Bayomi, Ibrahim Metwaly (2024) "Effect of Low-Flux versus High-Flux Dialyzers on Interleukin 6 (IL-6) Level in Patients Undergoing Maintenance Haemodialysis," *Al-Azhar International Medical Journal*: Vol. 5: Iss. 1, Article 16.
DOI: https://doi.org/10.58675/2682-339X.2196

ORIGINAL ARTICLE

Effect of Low-flux Versus High-flux Dialyzers on Interleukin 6 (IL-6) Level in Patients Undergoing Maintenance Hemodialysis

Hussein Salem Farahat Salem [a], Mohamed Nabil Raafat [a,*], Ismail Mohamed El Mancy [a], Ibrahim Metwaly Bayomi [b]

[a] Department of Internal Medicine, Faculty of Medicine, Al-Azhar University, Cairo, Egypt
[b] Clinical Pathology, Faculty of Medicine, Al-Azhar University, Cairo, Egypt

Abstract

Background: **One of the leading causes of death and suffering in the 21st century is chronic kidney disease (CKD). Due to the rise in risk factors like obesity and diabetes, as well as the rising number of people affected with CKD, our study aimed to study the effect of using low-flux compared with high-flux dialyzers on serum Interleukin-6 (IL-6) levels in patients undergoing regular hemodialysis (HD).**

Patients and methods: **Our study was a randomized controlled trial. Sixty patients were enrolled: 20 CKD patients, 20 dialysis patients using low-flux, and 20 patients using high-flux polysulfone dialyzers. Dialysis sessions were 4 h, 3 times weekly; the Anticoagulant was Heparin or LMWH.**

Results: **We found significantly (P=0.047) higher levels of serum IL-6 in HD patients (2.75±0.50 ng/l) than in CKD patients (2.49±0.38 ng/l). We also observed significantly higher IL-6 levels after dialysis (P=0.010) in the low-flux HD group. It was (2.68±0.36 ng/l) postdialysis versus (2.95±0.26 ng/l) predialysis. Finally, we found a statistically insignificant difference (P=0.491) in IL-6 levels after dialysis in the high-flux HD group. It was (3.02±0.57 ng/l) postdialysis versus (2.93±0.89 ng/l) predialysis.**

Conclusion: **Patients on hemodialysis had serum IL-6 levels that were considerably greater than those with CKD. After dialysis, there were noticeable increases in serum IL-6, especially when low-flux dialyzers were used. Utilizing high-flux dialyzers revealed a slower rise in IL-6, which may point to improved clearance.**

Keywords: Hemodialysis, High-flux dialyzers, Interleukin-6, Low-flux

1. Introduction

Renal replacement therapy in both forms; dialysis and kidney transplantation, has become prevalent. These treatments are used on more than a million patients with end-stage renal disease (ESRD) each year.[1] ESRD is characterized by vascular calcification, wasting, oxidative stress, and persistent inflammation brought on by endothelial dysfunction.[2] In ESRD, inflammation is a multifactorial process. Due to a combination of an impaired immune response brought on by a uremic state and persistent inflammatory stimulation due to blood membrane contact, water quality, biocompatible membranes, and vascular access, patients on dialysis experience persistent system stimulation, low-grade systemic inflammation, and altered cytokines balance.[3]

Serological evidence of an active inflammatory response in many hemodialysis (HD) and peritoneal dialysis patients is provided by elevated levels of nonspecific inflammatory markers and pro-inflammatory cytokines, such as interleukin-6 (IL-6). Serum albumin and C-reactive protein (CRP), both of which are acknowledged as major predictors of death in ESRD, are the prototypes of this reaction.[4]

Accepted 19 September 2023.
Available online 15 March 2024

* Corresponding author at: Department of Internal Medicine, Faculty of Medicine, Al-Azhar University, Nasr City, Cairo, 11651, Egypt.
E-mail address: hussein.farahat80@gmail.com (H.S.F. Salem).

https://doi.org/10.58675/2682-339X.2196

Similar studies found that plasma IL-6 levels are a strong predictor of death in HD patients.[5]

A crucial component of infection, autoimmune illness, and cancer is IL-6. One of the most closely regulated mediators of inflammation, it can increase under certain conditions from 1 to 5 pg/ml to multiple pg/ml. IL-6 is one of the most important factors in the hepatic acute-phase response and is essential for inflammation.[4]

As a result of its ability to control the acute-phase response and lymphocyte activation, IL-6 was once referred to as cytotoxic T-cell differentiation factor, interferon 2, B-cell differentiation factor, hepatocyte stimulating factor, and B-cell stimulatory factor-2.[6] The hypothalamic-pituitary-adrenal axis, glucose metabolism, mood, weariness, depression, and hematopoiesis are all under the influence of IL-6.[7] For instance, iron homeostasis is disrupted and iron-limited erythropoiesis and anemia are the results of hepatic control of hepcidin expression in response to systemic elevations in IL-6.[8]

Due to its wide range of biological functions, which include the ability to mediate the onset of malnutrition,[9] IL-6 has received a lot of attention in the context of ESRD. Despite the lack of a clear pathophysiological connection between inflammation and malnutrition, it has been demonstrated that serum IL-6 causes insulin resistance, protein catabolism, lipolysis, and appetite suppression.[10]

According to studies, uremia helps to keep elevated plasma IL-6 concentrations under control. Thus, the clinical management of end-stage renal illness is anticipated to be improved by specific anticytokine therapies combined with therapeutic control of IL-6, which will likely reduce numerous problems.[11] Some acute or chronic complications associated with maintenance HD, such as hypertension, anorexia, fever, muscle atrophy, osteoporosis, amyloid degeneration, etc., are believed to be caused by cytokines like IL-6 and interleukin-8 (IL-8), which are primarily derived from peripheral blood mononuclear cells (PBMC).[12]

The type of dialysis membrane employed by HD patients affects how cytokines production is induced. As a result, cytokines levels are frequently utilized as a gauge of a dialyzer's bio-compatibility. Prior to now, C3a, C5a, IL-1, and tumour necrosis factor alpha (TNF-α) have all been thoroughly investigated in relation to their potential participation in issues connected with HD that make use of dialyzers that are less bio-compatible. There have been a few investigations on the impact of different dialysis membranes on IL-6 generation, though.[13]

Our work aimed to study the effect of low-flux dialyzers in comparison with High-Flux Dialyzers on IL-6 levels pre and postdialysis in patients undergoing regular (three times/week) maintenance HD.

2. Patients and methods

Our study was a randomized controlled trial (RCT) at Al-Hussein Hospital and Saudi German Hospital Cairo, according to case availability. A total of 60 adult patients were enrolled; dialysis sessions duration were 4 h, three times weekly with polysulfone dialyzer membranes (Baxter TM); either 1.7/2.1 m^2 low flux or high flux dialysate ion concentrations were: K 2 mmol/l, Ca 1.50 mmol/l, Na 140 mmol/l and HCO3 32 mmol/l), and blood flow rates ranged from 250 to 300 ml/min. Dialysate flow rate was 500 ml/min. Ultrafiltration adjusted according to patients' dry weight, and anticoagulants used were low molecular weight heparin or heparin. All patients enrolled achieved Kt/V above 1.2 for 3 months calculated by using the Daugirdas formula, and controlled diabetes (HbA1c 7% on routine anti-diabetic therapy) were the inclusion criteria needed. Only adult patients (>18 years old); diagnosed with end stage kidney disease/National Kidney Foundation (NKF) guidelines, regular three times/week hemodialysis sessions for 3 months, the average duration of a single hemodialysis session was 240 min+−30. Our study excluded patients if they have: chronic liver disease (whatever the cause), severe thyroid dysfunction, active malignancies or active immunological disease, patients taking corticosteroids, immunosuppressive drugs or hormonal therapy, peritoneal dialysis and recent kidney transplant rejection, or signs of infection (hs-CRP≥10 mg/l; TLC ≥11 G/l).

2.1. Methodology

The study population was categorized into three groups: group I consisted of 20 patients who received HD treatment using 1.7 or 2.1 Low-flux polysulfone dialyzers; group II, 20 patients received HD treatment using 1.7 or 2.1 High-flux polysulfone dialyzers; group III, the control group; 20 patients not on dialysis (CKD stage 4). Every patient is given a thorough history, through physical examination, calculation of estimated glomerular filtration rate (GFR) using the modification of diet in renal disease (MDRD) study equation, basic investigations (complete blood count, urea, creatinine, potassium, phosphorus, sodium, calcium, HBA1c, alanine transaminase (ALT), aspartate transaminase (AST), Serum Albumin and CRP), pelvic abdominal ultrasound (to exclude liver cirrhosis or signs of chronic liver disease), and measurement of baseline levels of IL-6. After 3 months for groups I and II, basic

investigations and IL-6 levels pre- and post-mid-week HD sessions were performed.

Blood samples and IL-6 measurement: IL-6 levels in blood samples from CKD patients and hemodialysis patients were examined. Before and after the sessions, blood samples were taken from the venous line. The sandwich ELIZA test method was used to determine the amount of IL-6 in the serum. The Cobas-e-602 immunoassay analyzer (Roche Diagnostics, USA) was utilized with the BT LAB Human Interleukin 6 IL-6 ELIZA E0090Hu kit. This assay's analytical sensitivity was 1.03 ng/l. The samples were examined in accordance with the manufacturer's instructions (BT LAB, China supplied the human kit).

Analytical summary: the baseline descriptive data is illustrated using the mean (SD). Based on before (T0) and after (T480) dialysis findings, reduction ratios (RR) were calculated for each research variable using the formula RR (%) = [1 (T0/T480)] 100. The variation in mean RR between the study dialyzers was investigated using paired *t*-tests. All results were regarded as statistically significant when the *P* value was less than 0.05. The analysis was done using IBM SPSS 29 (Australia).

3. Results

Sixty patients with 140 measurements were included in our study. Included patients grouped into 20 CKD patients and 40 HD patients (18 patients dialyzed with low-flux dialyzers and 22 patients dialyzed by high-flux dialyzers); two patients were shifted from low- to high-flux dialyzer 1 month after starting this study.

Comparison between control group and HD group regarding IL-6 level at baseline, it showed statistically significant (*P* value 0.047) higher level in HD group (2.75±0.50 ng/l) versus control group (2.49±0.38 ng/l); Table 1.

Comparison between pre and postdialysis IL-6 level in low-flux HD groups showed a statistically significant value (*P* value 0.010) higher level in Sr. IL-6 postdialysis (2.95±0.26 ng/l {2.4–3.5}) versus Predialysis (2.68±0.36 ng/l {1.9–3.4}) Table 2.

A comparison between pre and postdialysis IL-6 levels in the high-flux HD group showed a statistically insignificant value (*P*=0.491) in Sr. IL-6 postdialysis (3.02±0.57 ng/l {1.9–5.1}) versus predialysis (2.93 ± 0.89 ng/l {1.8–6.5}). This also means its increase, but at a lower rate than in the low-flux group (Table 3).

A statistically significant (*r*=0.589; *P*=0.010) positive correlation observed between IL-6 and age of the patients in the low-flux HD group (Table 4).

An inverse correlation was found between age and the difference in IL-6 levels pre and postdialysis in the same group of low-flux HD patients (r=−0.580; *P*=0.012) (Table 5).

Table 1. Comparison between control and hemodialysis group regarding Interleukin-6 level at baseline.

IL-6 baseline	Control group	Patients group	Test value	*P* value	Significance
	No.=20	No.=40			
Mean ± SD	2.49±0.38	2.75±0.50	−2.026•	0.047	S
Range	1.8–3.1	1.6–4.9			

P value less than 0.05: (S) Significant; *P* value greater than 0.05: (NS) Nonsignificant; *P* value less than 0.001: (HS) Highly significant. •: Independent *t*-test.

Table 2. Comparison between Interleukin-6 predialysis and postdialysis among cases used low -flux filter group.

	Low-flux filter		Test value	*P*-value	Significance
	Predialysis	Postdialysis			
IL-6					
Mean ± SD	2.68±0.36	2.95 ± 0.26	−2.882•	0.010	S
Range	1.9–3.4	2.4–3.5			

P value less than 0.05: (S) Significant; *P* value greater than 0.05: (NS) Nonsignificant; *P* value less than 0.001: (HS) Highly significant; •: Paired *t*-test; ≠: Wilcoxon Ranks test.

Table 3. Comparison between Interleukin-6 predialysis and postdialysis among cases used high-flux filter group.

	High-flux filter		Test value	*P*-value	Significance
	Predialysis	Postdialysis			
IL-6					
Mean±SD	2.93±0.89	3.02±0.57	−0.701•	0.491	NS
Range	1.8–6.5	1.9–5.1			

P value less than 0.05: (S) Significant; *P* value greater than 0.05: (NS) Nonsignificant; *P* value less than 0.001: (HS) Highly significant; •: Paired *t*-test.

Table 4. The correlation between Interleukin-6 level and studied parameters pre dialysis among the hemodialysis patients.

	Interleukin-6pre dialysis			
	Low filter		High filter	
	r	*P*-value	*r*	*P*-value
Age	**0.589***	**0.010**	0.096	0.671
Weight (kg)	0.134	0.596	0.231	0.301
Albumin	0.254	0.310	−0.025	0.912
Hemoglobin	0.236	0.345	0.190	0.398
TLC	−0.103	0.683	0.039	0.864
S. Urea	−0.082	0.748	−0.076	0.736
S. Creat	−0.211	0.401	−0.199	0.375
eGFR	−0.104	0.683	0.159	0.481
Na	−0.120	0.635	0.324	0.141
K	0.083	0.744	0.050	0.826
Ca	0.165	0.513	0.090	0.690
Po4	−0.142	0.573	−0.307	0.164
HbA1c	0.172	0.495	−0.326	0.139
PTH	−0.215	0.392	−0.050	0.825
ALT	−0.010	0.967	0.379	0.082
AST	0.039	0.878	0.387	0.075
CRP	−0.196	0.436	0.016	0.943

Spearman correlation coefficient. ALT, alanine transaminase; AST, aspartate transaminase.

The earlier receiver operating characteristic curve demonstrates that the optimal cut off point for significant IL-6 at baseline in CKD and HD found greater than 2.5 with specificity 55%, sensitivity 77.5% and (AUC) area under curve 67% (Fig. 1).

4. Discussion

In our study, we found a significant difference (P=0.047) in baseline serum IL-6 levels in HD patients in comparison to control CKD patients; it was higher IL-6 Levels in the HD group (2.75±0.50 ng/l) versus (2.49±0.38 ng/l) in the control CKD group. The median age of HD patients was 65.85±12.58 year versus 62.15±15.61 years in the control CKD subjects; the Gender for HD patients was (female:15; male:25) versus (female:11, male:9) in the control CKD group. It also showed a significant (P=0.014) higher body weight in the HD group (82.08±17.07 kg) than in the control group (71.30±11.49 kg). This may have an impact on serum creatinine and IL-6 levels, as shown later in correlations, and also determines the type of filter, as a higher patient weight requires high-flux dialyzers. DM and HTN were the dominant causes of original kidney disease in HD patients (50%-20 patients; 30%-12 patients), respectively.

Table 5. The correlation between differences of Interleukin-6 pre and postdialysis.

	Interleukin difference			
	Low-flux filter		High-flux filter	
	r	*P*-value	*r*	*P*-value
Age	**−0.580***	**0.012**	−0.004	0.986
Weight (kg)	−0.289	0.245	0.020	0.931
Albumin	0.119	0.639	0.232	0.300
Hemoglobin	0.417	0.085	0.224	0.316
TLC	−0.205	0.414	−0.197	0.379
S. Urea	0.159	0.530	−0.035	0.876
S. Creat	0.219	0.383	0.165	0.463
eGFR	**−0.579***	**0.012**	−0.196	0.381
Na	0.195	0.438	0.376	0.085
K	0.385	0.114	0.194	0.388
Ca	−0.024	0.925	−0.108	0.632
Po4	0.148	0.557	−0.391	0.072
HbA1c	0.070	0.783	−0.357	0.102
PTH	−0.078	0.758	−0.092	0.684
ALT	0.121	0.632	−0.211	0.347
AST	0.204	0.417	−0.103	0.647
CRP	0.088	0.730	−0.358	0.102

Spearman correlation coefficient. ALT, alanine transaminase; AST, aspartate transaminase.

Our first finding was consistent with earlier research; Borazane *et al.*[14] they measured serum CRP, TNF-α, IL-6, and IL-10 in 30 patients who were diagnosed ESRD treated with CAPD: 16 patients (9 females, 7 males), HD: 14 patients (8 females, 6 males), before starting dialysis and after starting CAPD or HD by 3 months and in patients who show no symptoms of infection.

Twenty healthy people of equal ages and sexes made up the control group in the study by Borazane *et al.* ELIZA was used to measure the serum levels of IL-10, TNF-α, CRP, and IL-6. They came to the conclusion that compared with control people, CAPD and HD patients had greater serum levels of certain cytokines like IL-6 and CRP. However, over the course of three months, renal replacement treatment had no impact on the levels of blood cytokines and CRP.

Our study was similar to Borazane *et al.* study in patient characteristics and time frame, but contradicts in the control group where it was CKD patients in our study vs. healthy subjects; it also contradicts our finding regarding a high-flux membrane where it was not tested in the Borazane study.

Our findings were supported by a cross-sectional research by Alwahaibi *et al.*[15] that included 152 participants and measured IL10, IL6, and TNF-α to quantify inflammation. 54 healthy participants, 45 recipients of renal transplants, and 53 HD patients were enrolled. Serum IL6 levels were substantially higher in dialysis patients than in the healthy participants (40.241.4 vs. 16.45.4 pg/ml; P 0.05), but kidney transplant patients and healthy subjects did not differ significantly from one another. They came to the conclusion that; renal transplant patients had higher levels of IL10 and TNF-α than healthy controls, while HD patients had higher inflammatory

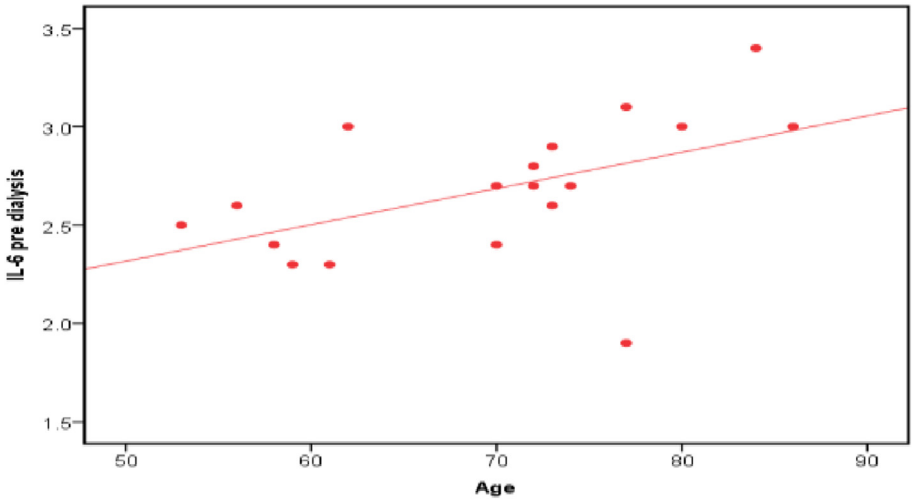

Figure 1. Correlation between IL-6 and age of the hemodialysis patients.

markers levels (TNF-α and IL6) than healthy controls.

Alwahaibi *et al.* study contradicts our study in control group; healthy people and the levels of IL-6 were same. Pre versus postHD unlike our finding. Another important difference was that they did not measure CRP, an important marker for ruling out concurrent infections.

Our results, however, do not agree with Kamimura *et al.*[16] study, they examined levels of IL-6 in HD patients and healthy individuals. For evaluation of energy expenditure and serum IL-6, Kamimura' study included 80 HD patients in a cross-sectional study. The endotoxin-stimulated and spontaneous production of IL-6 by PBMCs was tested in a subgroup of 30 HD patients and 11 healthy control individuals. IL-6 levels were assessed using the ELIZA test. By using indirect calorimetry, the resting energy expenditure is calculated. Between patients and control participants, there were no discernible differences in the levels of IL-6 produced by PBMCs (spontaneous production, 6541 (96–7739) pg/ml vs. 3410 (50–7806) pg/ml and stimulated production, 6530 (579–7671) pg/ml vs. 5304 (1527–7670) pg/ml).

Unlike study by Kamimura *et al.*;[16] where the HD patients' median age was 43.1±14.2 years; and the control group was healthy people, with median body weight of 62.7±13 kg. In our study; the median age was 65.85±12.58 years; patients with CKD made up the control group and the median body weight was 82.08±17.07.

The second finding in our study was that the comparison between pre dialysis and post dialysis IL-6 levels in the low-flux HD group showed a statistically significantly higher value (P=0.010) in Serum IL-6 post-dialysis (2.95±0.26 ng/l {Range:2.4–3.5}) vs. pre-dialysis value (2.68±0.36 ng/l {Range:1.9–3.4}).

This finding was in concordance with recent cross-sectional study published by Wibowo *et al.*;[17] 20 patients were included. Inclusion criteria were: CKD patients undergoing regular HD greater than or equal to 3 years, only adults with informed consent included. Study patients underwent: history taking, physical examination, anthropometric measurements, and laboratory tests for albumin, creatinine, hemoglobin, and IL-6. Wibowo *et al.* found that serum IL-6 levels post HD significantly increased (10.39 pg/ml before HD and 29.13 pg/ml after HD). The link between HD and IL-6 levels before and after HD was therefore determined to be statistically significant (P=0.006). They came to the conclusion that IL-6 levels before and after routine hemodialysis in CKD patients had a statistically significant relationship.[17]

Likewise, the analytic cross-sectional study by Zahed and Chehrazi[18] on HD patients who experienced metabolic acidosis; it included 84 patients in HD wards of Ashrafi Esfahani and Loghman Hakim Hospitals. Patients were on dialysis trice/week for more than 3 months, along with stable state during that period, were requirements for inclusion. The exclusion criteria for that study were BMI greater than 35, use of cortico-steroids, intravenous antibiotics, or dialysis duration of less than 3 months, and causes of hypercatabolic states (such as infection, inflammation).

The demographic data were quite similar to those of our study, including age, sex, type of vascular access, presence of diabetes, quality and duration of dialysis. IL-10 and IL-6 concentrations were measured using ELIZA kits. Hemoglobin, platelets,

white blood cells, parathyroid hormone, calcium, phosphorus, ferritin, serum albumin, CRP, transferrin, venous blood gas, creatinine and blood urea nitrogen levels were tested before mid-week HD in a single laboratory test. Serum IL-6 in average was 6.036 pg/ml versus (2.68±0.36 ng/l) in our study, Zahed *et al.* did not measure IL-6 postdialysis.

However, our findings were not in line with those of Memoli *et al.,*[19] who investigated IL-6 release in the supernatant of 24 h cultured PBMC from: (A) 10 HD patients, (B) seven advanced CKD patients (GFRs 10 ml/mm) and (C) eight control healthy individuals. They examined the connection between the synthesis of IL-6 and the generation of beta-2 microglobulin. Blood samples from HD patients were taken before and after the following periods of dialysis: (1) after 2 months of poly-methyl-methacrylate (PMMA) membrane dialysis, (2) after 1 and 2 months of Cuprophan membrane dialysis and (3) after 1 more month of Cuprophan membrane dialysis. HD patients receiving Cuprophan membranes demonstrated significantly increased levels of IL-6 production pre (23 13 U/3×106 PBMC/24 h) and post (26.2 11.3 U/3×106 PBMC/24 h) dialysis session as compared with control individuals (6.0 5.6 U/3×106 PBMC/24 h). When patients were dialyzed using PMMA dialyzers; IL-6 levels at the beginning of dialysis did not substantially differ from those seen in controls (10.6 4 U/3 10 PBMC/24 h and 7.8 U/3 106 PBMC/24 h, respectively, after 1 month of HD).

After 1 month of dialysis; patients switched back to use Cuprophan dialyzers (CU2, 44.6 9, 4 U/3 106 PBMC/24 h), their IL-6 production skyrocketed, reaching levels noticeably higher than levels attained during the initial period while using Cuprophan dialyzers. They concluded that; there was no change in production levels of IL-6 measured prior to and following dialysis using PMMA or Cuprophan dialyzers. We used polysulfone membrane for HD in our study as opposed to cuprophan or PMMA in Memoli *et al.*'s work.[19]

Another recent prospective single-center study by Quiroga *et al.* (2021)[20] studied the relationship between mortality in coronavirus disease 2019 (COVID-19) and IL-6 dynamic measurment during HD, study included 16 COVID-19-positive HD patients. Using a PMMA dialyzer. Prior to, following, and 1 week after the first HD session, IL-6 levels were assessed. Between survivors and nonsurvivors, laboratory results, baseline comorbidities, chest radiography and medications were noted and compared. Four (25%) of the 16 patients, 13 male with average age 72±15 years died. Length of time on dialysis (P=0.01), infiltrates in CXR (P=0.032), CRP (P=0.05), oxygen need (P=0.02), LDH (P=0.02) at 1 week and anticoagulation (P 0.01) were the factors linked to death. Nonsurvivors did not exhibit the same reduction in IL-6 levels during the session (using PMMA filter) as what was observed in survivor patients; survivors showed a 25% reduction [17.5–53.2] versus nonsurvivors: 2.8% reduction [109.4–12.8], P=0.04 for both. Nonsurvivors also had higher levels before and after dialysis IL-6 at admission (P=0.02 for both). The survivors' IL-6 levels before dialysis were 6.3 pg/ml (0.5–35.3) and after dialysis were 3.8 pg/ml (1.8–27.0). IL-6 levels before dialysis in nonsurvivors were 45.7 pg/ml (18.1–87.9) while after dialysis were 57.6 pg/ml (14.8–140.7).

Quiroga *et al.*[20] concluded that; in regular HD COVID19 patients, a positive IL-6 balance during the entry HD session was linked to greater mortality. There were certain restrictions on that study; it was a single-center study, like other COVID-19'studies in dialysis patients, the sample size was limited. Due to these factors, several differences that were clinically significant did not achieve statistical significance. Despite these limitations, the findings provide critical information about risk stratification in unstudied group. Second, they were unable to evaluate other inflammatory indicators including IL-8, TNF-α or IL-17. The COVID-19 cytokine storm appears to be primarily mediated by IL-6, which is frequently detected in clinical settings. Therefore, these discoveries might directly impact clinical practice. Third, because to technological limitations in their COVID HD equipment, they were unable to compare the outcomes in HF-HD with OL-HDF.

Our third impressive finding was that the comparison between before and after dialysis IL-6 levels in the high-flux HD group showed a statistically insignificant value (P=0.491); higher levels of IL-6 postdialysis (3.02±0.57 ng/l{1.9–5.1}) versus predialysis (2.93 ±0.89 ng/l{1.8–6.5}); so the rate of increase postdialysis was lower than what is happened in low-flux group (IL-6 postdialysis (2.95±0.26 ng/l{2.4–3.5}) vs. predialysis value (2.68±0.36 ng/l {1.9–3.4}) (P value 0.010).

This important finding indicates a better clearance of IL-6 when using a high-flux dialyzer during dialysis. Although the fact that the high-flux group's mean body weight was substantially greater (88.95±15.63 kg vs. 73.67±15.20 kg in Low-flux group; P value 0.003; highly significant) but the difference between its levels pre and postdialysis was Clearly evident to be lesser when using high-flux dialyzers.

4.1. Conclusion

Patients on HD had serum IL-6 levels that were considerably greater than those with CKD. After

dialysis, there were noticeable increases in serum IL-6, especially when low-flux dialyzers were used. Utilizing high-flux dialyzers revealed a slower rise in IL-6, which may point to improved clearance.

Conflicts of interest

There are no conflicts of interest.

References

1. Rosa-Diez G, Gonzalez-Bedat M, Pecoits-Filho R, et al. Renal replacement therapy for Latin American end-stage renal disease. *Clin Kidney J*. 2014;7(4):431–436.
2. Podkowińska A, Formanowicz D. Chronic kidney disease as oxidative stress-and inflammation-mediated cardiovascular disease. *Antioxidants*. 2020;9:752.
3. Xu H, Huang X, Risérus U, et al. Dietary fiber, kidney function, inflammation, and mortality risk. *Clin J Am Soc Nephrol*. 2014;9(12):2104–2110.
4. Zimmermann J, Herrlinger S, Pruy A, Metzger T, Wanner C. Inflammation enhances cardiovascular risk and mortality in hemodialysis patients. *Kidney Int*. 1999;55(2):648–658.
5. Beberashvili I, Sinuani I, Azar A, et al. IL-6 levels, nutritional status, and mortality in prevalent hemodialysis patients. *Clin J Am Soc Nephrol*. 2011;6(9):2253–2263.
6. Tanaka T, Narazaki M, Kishimoto T. IL-6 in inflammation, immunity, and disease. *Cold Spring Harbor Perspect Biol*. 2014;6: a016295.
7. Ting EY, Yang AC, Tsai SJ. Role of interleukin-6 in depressive disorder. *Int J Mol Sci*. 2020;1:2194.
8. Schmidt PJ. Regulation of iron metabolism by hepcidin under conditions of inflammation. *J Biol Chem*. 2015;290: 18975–18983.
9. Stenvinkel P, Wanner C, Metzger T, et al. Inflammation and outcome in end-stage renal failure: does female gender constitute a survival advantage? *Kidney Int*. 2002;62(5): 1791–1798.
10. Kalantar-Zadeh K, Kilpatrick RD, Kuwae N, et al. Revisiting mortality predictability of serum albumin in the dialysis population: time dependency, longitudinal changes and population-attributable fraction. *Nephrol Dial Transpl*. 2005; 20(9):1880–1888.
11. Imig JD, Ryan MJ. Immune and inflammatory role in renal disease. *Compr Physiol*. 2005;3:957.
12. Kany S, Vollrath JT, Relja B. Cytokines in inflammatory disease. *Int J Mol Sci*. 2019;20:6008.
13. Lonnemann G, Haubitz M, Schindler R. Hemodialysis-associated induction of cytokines. *Blood Purif*. 1990;8:214–222.
14. Borazan A, Ustün U, Ustundag Y, et al. The effects of peritoneal dialysis and hemodialysis on serum tumor necrosis factor-alpha, interleukin-6, interleukin-10, and C-reactive protein levels. *Mediators Inflamm*. 2004;13(3):201–204.
15. Alwahaibi NY, Alissaei HK, Alshihi SA, Alabri N, Albalushi SS, Albalooshi M. Serum levels of TN F-α, IL-6 and IL-10 in haemodialysis and renal transplant patients and in healthy subjects. *Port J Nephrol Hypert*. 2016;30:194–198.
16. Kamimura M, Draibe S, Dalboni M, et al. Serum and cellular interleukin-6 in haemodialysis patients: relationship with energy expenditure. *Nephrol Dial Transplant*. 2007;22(3): 839–844.
17. Wibowo AT, Alwi TN, Putri CE. The relationship between HD procedures and IL-6 levels in regular HD patients in Haji Adam Malik Central general Hospital. *Int J Res Rev*. 2021;8: 1–5.
18. Zahed N, Chehrazi S. The evaluation of the relationship between serum levels of Interleukin-6 and Interleukin-10 and metabolic acidosis in hemodialysis patients. *Saudi J Kidney Dis Transplant*. 2017;28:23.
19. Memoli B, Postiglione L, Cianciaruso B, et al. Role of different dialysis membranes in the release of interleukin-6-soluble receptor in uremic patients. *Kidney Int*. 2000;58(1):417–424.
20. Quiroga B, Muñoz-Ramos P, Giorgi M, de Santos A, Núñez A, Ortiz A. Dynamic assessment of interleukin-6 during hemodialysis and mortality in coronavirus disease-19. *Ther Apher Dial*. 2021;25(6):908–916.