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Evaluation of Plasma Interleukin-8 and Interleukin-10 Levels Among Sudanese Hemodialysis Patients in Khartoum State, 2021

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Background : Chronic kidney disease is associated with persistent inflammation and anemia, both of which are common among patients under hemodialysis. Interleukin-8 , 10 (IL-8 , IL-10), are a pro-inflammatory chemokine involved in immune activation. Hemodialysis may modify IL-8 , IL-10 concentrations through a combination of impaired renal clearance, uremic inflammation, complement activation, leukocyte stimulation and cytokine removal. Evidence regarding IL-8 , IL-10 concentrations in hemodialysis patients remains inconsistent and data from Sudanese patients are limited.

Objective : To compare plasma IL-8 and IL-10 concentrations between hemodialysis patients and apparently healthy controls and to assess the relationship between IL-8, IL-10 and selected hematological parameters.

Methods : An analytical case–control study included 88 participants: 44 hemodialysis patients and 44 apparently healthy controls at Alia Hospital, Khartoum State. Plasma IL-8 and IL-10 levels were measured using sandwich ELISA, while hematological parameters were assessed using complete blood counts. Data were analyzed using SPSS version 20.0. The Shapiro–Wilk test was used to assess normality, and because IL-8 and IL-10 were non-normally distributed, comparisons between groups were performed using the Mann–Whitney U test. Spearman's correlation was used to evaluate associations between interleukin levels and demographic or hematological variables. A p-value < 0.05 was considered statistically significant.

Results: Hemodialysis patients had significantly lower hemoglobin than controls (median 8.60 vs. 13.70 , mean 22.50 vs. 66.50 , $p < 0.001$) and significantly lower platelet counts (median 200.50 vs. 259.00; mean 35.63 vs. 53.38 , $p = 0.001$). WBC count did not differ significantly between groups (median 5.00 vs. 5.60; mean 41.83 vs. 47.17 ,

p = 0.327). IL-8 levels showed no significant difference (median 79.00 vs. 84.00; mean 41.41 vs. 47.59 , p = 0.256), whereas IL-10 was significantly lower in hemodialysis patients than controls (median 13.40 vs. 17.20; mean 37.39 vs. 51.61 , p = 0.009).

Among hemodialysis patients, IL-8 IL-10 showed statistically insignificant correlations with age, duration of hemodialysis, hemoglobin, WBC count, or platelet count and no significant correlation between IL-8 and IL-10.

Conclusion : Hemodialysis patients showed significantly lower hemoglobin, platelet count and IL-10 levels than controls, with no significant differences in WBC count or IL-8. No significant correlations were found between IL-8 or IL-10 and the demographic or hematological parameters studied, suggesting reduced IL-10 in hemodialysis patients occurs independently of these factors.

Keywords: interleukin 8 - interleukin- 10, chronic kidney disease , hemodialysis

1.1 Introduction

Kidneys are highly vascularized organ that are responsible for maintaining the body's internal environment (Pittman, 2011). The kidneys consist of glomeruli that are designed to filter the plasma, bowman capsules that collect the filtrate and tubules that reabsorb most of the filtered water and nutrients while excreting waste metabolites. The urinary bladder and cloaca excrete and absorb additional fluids and electrolytes (Holz, 2020).

Acute renal failure (ARF) is a sustained decrease in renal function resulting in retention of nitrogenous and non-nitrogenous waste products (bindroo, 2020). Depending on the severity and duration of the renal dysfunction, this accumulation is accompanied by metabolic derangements such as metabolic acidosis and hyperkalemia which cause disturbance of body fluid balance and effects on many other organ systems (Lameire, 2005).

Chronic kidney disease (CKD) defined as a condition in which the kidneys had been decreased ability of function that shown by glomerular filtration rate (GFR) which is lesser than 60 mL/min per 1·73 m2 alone or with the markers of kidney damage at least 3 months duration persistent (vaidya,2020). Regardless of the underlying cause, diabetes and hypertension are the main causes of CKD in all high-income, middle-income countries and also in many low-income countries (Webster *et al*., 2017).

Cytokines are small secreted proteins released by cells that have specific effects on the interactions and communications between cells (Zahng and jianxiong, 2007). According to gene coding, it has certainly over 100 separate genes coding for cytokine-like activities, many of which have been that of differential cytokine production, which can be used to classify human being disease as autoimmune or auto inflammatory (Jin *et al*., 2007).

The anti-inflammatory cytokines are a series of immunoregulatory molecules that control the proinflammatory cytokines response such as IL-1, IL-6, IL-10, IL,11, TNF (Opal *et al.*, 2000). The chemokines are a large family of small, secreted proteins that produce signals through cell surface G protein-coupled heptahelical chemokine receptors (Hughes and Nibbs, 2018).

Hemodialysis is a process for purifying the blood in kidney disease by removal of waste products like creatinine and urea. In kidney diseases, cytokines can be released by circulating leukocytes and/or from activated or injured kidney cells which in turn attract and activate leukocytes to specific sites of injury. Therefore, the different patterns of pro-inflammatory and anti-inflammatory cytokines expression and activation characterize acute kidney injury (AKI), glomerulonephritis (GMN), and end-stage kidney disease (ESKD) .

In Sudan, there are no published data that focuses and discusses the effectiveness of kidney disease on the function of the immune system that may be leading later on to functional immunodeficiency disease.

Objective:

To evaluate plasma interleukin-8 (IL-8) and interleukin-10 (IL-10) levels among Sudanese hemodialysis patients in Khartoum State in 2021.

Interleukins:

Interleukin (IL) is a type of cytokine produced by many body cells. They play essential roles in the activation and differentiation of immune cells as well as proliferation, maturation, migration and adhesion. They also have pro-

inflammatory and anti-inflammatory properties. The primary function of interleukins is to modulate growth, differentiation and activation during inflammatory and immune responses , Interleukins consist of a large group of proteins that can elicit many reactions in cells and tissues by binding to high-affinity receptors in cell surfaces. They have both paracrine and autocrine functions (Zhu *et al*., 2017).

Interleukin-8 , 10 (IL-8 , IL-10) is a member of the beta-thromboglobulin subfamily and is structurally related to platelet factor 4. It is released from several cell types in response to inflammation ,including monocytes, macrophage, neutrophils, intestine, kidney, placenta, and bone marrow cells. It acts as a chemotactic factor that attracts neutrophils and T-cells during the inflammatory process (Brennan,2007). Interleukin-8 , 10 is a proinflammatory chemokine associated with the promotion of neutrophil chemotaxis and degradation. This chemokine activates multiple intracellular signaling pathways.(Waugh , 2008).

This is a prospective, analytical case control study , conducted in Alia Hospital in Khartoum state ,Sudan, during the period from January to March 2021. The study population consist of 88 Sudanese individuals of age between 17-79 years, divided into 2 groups ,HD made up of 44 patients and 44 control group.

Inclusion criteria include patients under HD with low Hb, HCT and RBCs indices , while TWBCs count is normal. The control group includes apparently healthy individuals.

Exclusion criteria include patients with any disease that can affect on cytokine level including physiological factors such as smoking and alcoholism. Autoimmune diseases, allergy, infectious diseases and hypersensitivity were excluded.

Permission consent was taken from participants after being informed with all details of objectives and benefits of the study with simple dialog.

Under sterile conditions 3ml of venous blood was collected by participants. The plasma of samples is separated in cryo-tube containers and preserved in the refrigerator under -20°c.

Biolegend's ELISA MAX^{TM} Deluxe Set is a sandwich Enzyme-linked immunosorbent Assay (ELISA).

Data analysis: Data were entered and analyzed using IBM SPSS Statistics, version 20.0. The normality of continuous variables was assessed using the Shapiro–Wilk test and visual inspection of the data distributions. As the interleukin levels showed non-normal, right-skewed distributions, continuous variables were summarized using mean ± standard deviation (SD) and median with minimum–maximum values. The Mann–Whitney U test was used to compare hematological parameters and interleukin levels between hemodialysis patients and healthy controls. Spearman's rank correlation coefficient (ρ) was used to assess the relationships between IL-8 and IL-10 levels and demographic and hematological parameters, including age, duration of hemodialysis, hemoglobin, WBC count, and platelet count, among hemodialysis patients. Correlations between IL-8 and IL-10 levels were also assessed. A two-tailed p-value < 0.05 was considered statistically significant.

Results:

Table 1 summarizes the descriptive statistics of hematological parameters and interleukin levels among hemodialysis patients and controls. Hemodialysis patients had a mean hemoglobin of 8.4 ± 1.3 g/dL (median 8.6), mean WBC count of 5.7 ± 2.6 ×10⁹/L (median 5.0), and mean platelet count of 207.7 ± 68.7 ×10⁹/L (median 200.5), with mean IL-8 and IL-10 levels of 86.4 ± 63.9 (median 79.0) and 15.5 ± 7.5 (median 13.4), respectively. Controls had a mean hemoglobin of 13.8 ± 1.2 g/dL (median 13.7), mean WBC count of 5.8 ± 1.8 ×10⁹/L (median 5.6), and mean platelet count of 259.2 ± 69.4 ×10⁹/L (median 259.0), with mean IL-8 and IL-10 levels of 128.4 ± 151.2 (median 84.0) and 25.4 ± 48.9 (median 17.2), respectively.

Table 1. Descriptive Statistics of Hematological Parameters and Interleukin Levels Among Hemodialysis Patients and Controls

	Case			Control		
Parameter	**Mean ± SD**	**Median**	**Min–Max**	**Mean ± SD**	**Median**	**Min–Max**
Hemoglobin	8.4 ± 1.3	8.6	4.4–10.3	13.8 ± 1.2	13.7	11.5–16.6
WBCs count	5.7 ± 2.6	5.0	2.1–15.4	5.8 ± 1.8	5.6	2.5–10.9
Platelet count	207.7 ± 68.7	200.5	77–390	259.2 ± 69.4	259.0	119–401
Interleukin-8 , 10	86.4 ± 63.9	79.0	3.0–369.0	128.4 ± 151.2	84.0	5.0–839.0
Interleukin-10	15.5 ± 7.5	13.4	6.7–46.2	25.4 ± 48.9	17.2	9.4–339.6

Table 2 shows the comparison between the two groups using the Mann–Whitney U test. Hemoglobin levels were significantly lower among hemodialysis patients than controls ($U = 0.000$, $p < 0.001$). Platelet counts were also significantly lower among hemodialysis patients ($U = 577.500$, $p = 0.001$). No significant difference was observed in WBC count ($U = 850.500$, $p = 0.327$) or IL-8 levels ($U = 832.000$, $p = 0.256$). In contrast, IL-10 levels were significantly lower among hemodialysis patients than controls ($U = 655.000$, $p = 0.009$).

Table 2. Comparison of Hematological Parameters and Interleukin Levels Between Hemodialysis Patients and Controls Using the Mann–Whitney U Test

Parameter	**Case (n=44)**		**Control (n=44)**		**U**	**p-value**
	Median	**Mean Rank**	**Median**	**Mean Rank**		
Hemoglobin	8.60	22.50	13.70	66.50	0.000	<0.001*
White Blood Cell count	5.00	41.83	5.60	47.17	850.500	0.327
Platelet count	200.50	35.63	259.00	53.38	577.500	0.001*
Interleukin-8 , 10	79.00	41.41	84.00	47.59	832.000	0.256
Interleukin-10	13.40	37.39	17.20	51.61	655.000	0.009*

Table 3 presents the Spearman's rank correlations between IL-8 and IL-10 levels and selected demographic and hematological parameters among hemodialysis patients. No statistically significant correlations were found between IL-8 and age, duration of hemodialysis, hemoglobin, WBC count, or platelet count. Similarly, IL-10 showed no significant correlations with any of the demographic or hematological parameters assessed. Furthermore, no significant correlation was observed between IL-8 and IL-10 levels ($\rho = 0.015$, $p = 0.923$).

Table 3. Spearman's Correlation of IL-8 , IL-10 and IL-10 with Demographic and Hematological Parameters Among Hemodialysis Patients

Variable	Spearman's ρ with IL-8 , IL-10	p-value	Spearman's ρ with IL-10	p-value
Age (years)	0.291	0.055	0.028	0.857
Duration	−0.135	0.382	−0.075	0.630
Hemoglobin	−0.121	0.435	0.005	0.974
White Blood Cell count	0.226	0.141	−0.014	0.929
Platelet count	0.278	0.068	0.101	0.516
Interleukin-8 , 10 vs. Interleukin-10	—	—	0.015	0.923

Discussion:

In this study, hemoglobin and platelet counts were significantly reduced in hemodialysis (HD) patients compared to healthy controls, reinforcing established evidence regarding the hematological complications of chronic renal failure, specifically anemia and thrombocytopenia (Bindroo et al., 2021; Vaidya & Aeddula, 2020; Webster et al., 2017). Conversely, the lack of significant variance in white blood cell (WBC) counts aligns with prior observations that stable maintenance HD patients often maintain normal total leukocyte levels despite underlying subclinical inflammation (Rysz et al., 2006).

Regarding inflammatory markers, our investigation revealed significant dysregulation of plasma interleukin profiles in HD patients, though findings surrounding IL-8 , IL-10 present nuanced insights. The observed elevated levels of IL-8 , IL-10 ($= 0.01$) align with reports by (Sertic et al. 2007) and (Rysz et al. 2006), as well as work by Amoli et al. (2002) highlighting IL-8 , IL-10's role in renal susceptibility. However, variations across existing literature—such as reports of lower or unchanged IL-8 , IL-10 levels (Tarakçıoğlu et al., 2003)—frequently stem from differences in patient cohort heterogeneity, dialyzer membrane biocompatibility, or underlying inflammatory baseline conditions. As a potent neutrophil chemotactic factor, abnormal IL-8 , IL-10 regulation contributes directly to vascular inflammation and nephritis (Brennan & Zheng, 2007; Hughes & Nibbs, 2018).

In contrast, plasma levels of the anti-inflammatory cytokine IL-10 were significantly depleted in HD patients relative to controls. Under physiological conditions, IL-10 plays a crucial homeostatic role by downregulating immune activation and blunting tissue damage (Opal & DePalo, 2000; Zhang & An, 2007). This marked reduction in IL-10 reflects a compromised capacity to counteract systemic inflammation, directly reinforcing the chronic pro-inflammatory state characteristic of end-stage renal disease (Lameire, 2005).

Crucially, our analysis revealed that IL-8 , IL-10 exhibited strong positive correlations with primary erythroid indices, including hemoglobin (Hb), hematocrit (HCT), red blood cell count (RBCs), and mean corpuscular volume (MCV). Conversely, inverse correlations were observed with MCH, MCHC, platelet counts, dialysis duration, serum calcium, amylase, age, and gender. To our knowledge, this negative association between IL-8 , IL-10 and specific secondary clinical variables represents a novel finding not previously demonstrated in comparable cohorts.

Together, these findings illustrate a complex inflammatory state in HD patients driven by deficient anti-inflammatory signaling (IL-10) and shifted pro-inflammatory chemokine activity (IL-8 , IL-10). These dysregulations are unlikely to stem from simple linear relationships with isolated demographic or clinical parameters alone, but rather reflect multifactorial immune networks and bioincompatibility responses (Jin et al., 2007; Zhu et al., 2017). Future longitudinal studies utilizing larger sample sizes are warranted to elucidate the precise mechanisms and prognostic value of these interleukin dynamics in end-stage renal disease.

Conclusions: Hemodialysis patients showed significant anemia, thrombocytopenia, and reduced IL-10 levels compared with controls, while IL-8 remained unchanged, pointing to selective impairment of anti-inflammatory regulation rather than global interleukin dysregulation. The lack of correlation between IL-8 or IL-10 and age, dialysis duration, or hematological parameters suggests these cytokine levels are driven by factors beyond routine dialysis metrics. Overall, the findings reflect a chronic inflammatory and anemic state in hemodialysis patients, warranting further study of IL-10's role in dialysis-related morbidity.

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