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Serum Interleukin-10 Levels and Microinflammation in Vascular Access Failure in Egyptian Children on Hemodialysis

M. F. Elshamama¹, S. Sabry², A. Galal¹, H. Koura¹, N. Kantoush³, M. Rasheed³, E. H. Thabet³

Background: Vascular access (VA) dysfunction is a major clinical complication in the hemodialysis population and has a direct effect on dialysis outcome. Neointimal hyperplasia causes vascular stenosis and subsequent thrombosis, which result in vascular access failure in patients undergoing hemodialysis. Interleukin-10 (IL-10) and C-reactive protein are involved in this inflammatory process. **The aim of this study** was to investigate the relationship between vascular access failure and IL-10 levels and to explore the role of microinflammation in the VA dysfunction in maintenance pediatric hemodialysis patients. **Methods:** Forty children receiving maintenance hemodialysis with an arteriovenous fistula in place or an artificial graft (AVG) or a tunneled permanent catheter (TPC) were included in this study. They were divided into two groups: group 1 (n = 26): children with good vascular access, and group 2 (n = 14): children with vascular access failure. Twenty healthy children were matched as controls for serum IL-10 and high-sensitivity C-reactive protein (hs-CRP) levels. Clinical and laboratory data including serum IL-10 and hs-CRP levels were compared. **Results:** Female gender, hypoproteinemia, and hypercholesterolemia were associated with vascular access failure. Serum IL-10 in group 2 was significantly higher than in group 1 and in controls (45.68 ± 29.62 pg/ml vs 31.07 ± 22.01 pg/ml and 12.70 ± 9.76 pg/ml; $p < 0.05$, and $p < 0.001$, respectively). Serum hs-CRP in group 2 was significantly higher than in group 1 and in controls (5.27 ± 5.44 mg/l vs 2.32 ± 2.30 mg/l and 1.36 ± 0.67 mg/l, $p < 0.01$ and $p < 0.005$, respectively). Moreover, serum hs-CRP levels were negatively correlated with IL-10 levels ($r = -0.36$; $p = 0.01$). Also, serum hs-CRP levels were negatively correlated with serum albumin ($r = -0.78$; $p = 0.04$), serum cholesterol ($r = -0.91$; $p = 0.002$) and fractional shortening percentage on cardiac echo ($r = -0.36$; $p = 0.01$). Multiple regression analysis confirmed AVG and TPC, cardiovascular disease, vascular access duration, and WBC as factors independently influencing CRP levels. **Conclusion:** Patients with VA dysfunction have significantly higher levels of serum IL-10 and hs-CRP. An altered immune response and microinflammation might contribute to vascular access failure. AVG and TPC have a higher degree of chronic inflammation than AVF. *J Clin Basic Cardiol* 2009; 12 (online): 18–23.

Keywords: interleukin-10, microinflammation, uremia, arteriovenous dysfunction, hemodialysis

Vascular access (VA) failure, the most frequent cause of morbidity and hospitalization in patients undergoing hemodialysis, is primarily due to vascular stenosis, which predisposes to thrombosis and subsequently leads to access obstruction. It is therefore quite important to fully understand the potential mechanisms underlying VA dysfunction [1].

Neointimal hyperplasia (NIH) is believed to be the predominant cause of vascular stenosis of both the arteriovenous fistula (AVF) and the polytetrafluoroethylene (PTFE) graft [1, 2]. The pathophysiology of NIH consists of an aberrant wound-healing process characterized by vascular smooth muscle cell (VSMC) migration, adherence, proliferation, and extracellular matrix deposition. The altered VSMC response is mediated in part by cytokines and growth factors. Tumor necrosis factor- α (TNF- α) stimulates the synthesis of other pro-inflammatory cytokines and adhesion molecules as it has a chemotactic activity for monocytes and stimulates migration and proliferation of VSMC. On the other hand, interleukin-10 (IL-10) exerts an anti-inflammatory activity, which inhibits inflammatory cytokines such as TNF- α and inactivates inflammatory cells [1, 2].

Recent studies have suggested that end-stage renal disease (ESRD) is associated with a chronic low-grade inflammatory state, also called microinflammation characterized by elevation of circulating proinflammatory cytokines, giving rise to the triad of malnutrition–inflammation–atherosclerosis, or the malnutrition, inflammation and atherosclerosis (MIA) syndrome. Microinflammation is also present in hemodialysis patients and is closely correlated to the morbidity and mortality of the dialysis patients, especially by increasing the incidence of cardiovascular events through initiation and

progression of atherosclerosis [3–6]. Elevated C-reactive protein (CRP) levels, markers of inflammation and low serum albumin, are well-known predictors of mortality in both renal and non-renal diseases [7].

Multiple studies over the past decade have consistently shown that even minor elevation in CRP increases the risk of cardiovascular events or stroke in apparently healthy-looking persons [8]. In ESRD patients, elevated levels of CRP are seen in more than a third of patients, which correlated as well with hypoalbuminemia, malnutrition, erythropoietin resistance, and thus increased mortality of patients. Although microinflammation has been documented to correlate well with cardiovascular events in ESRD patients [9–12], the relationship between microinflammation and AVF dysfunction is still to be clarified.

Aim

In this study, we assess the relationship between the anti-inflammatory marker IL-10 level and vascular access failure and evaluate the influence of this marker on the development of vascular access failure and investigate the possible association between microinflammation (as represented by the hs-CRP level) and AV dysfunction in maintenance hemodialysis pediatric patients.

Patients and Methods

From June 2008 to January 2009, 40 pediatric patients on maintenance hemodialysis at the Hemodialysis Unit of the Center of Pediatric Nephrology and Transplantation (CPNT), Children Hospital, Cairo University were selected for this

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study. Their creatinine clearance was < 10 ml/min/m². Patients with hepatic disease, peptic ulcer, asthma, infection, tumor, febrile, congestive heart failure, and other acute inflammatory diseases were excluded from this study. Children who were matched for the above criteria were divided into two groups according to their VA functional state: group 1 ($n = 26$): children treated with routine HD with well-functioning VA; group 2 ($n = 14$): hemodialysis patients with VA dysfunction.

All native AVF were set up by surgical anastomosis of the radial (wrist) or brachial (elbow and upper arm) artery to the cephalic vein. Ultrasound was used to quantify the diameters of the artery and vein, and to exclude stenosis or thrombosis of the draining vein. Fistulas were placed preferentially to grafts, and required a minimum artery diameter of 2 mm and a minimum vein diameter of 2.5 mm. Graft placement (AVG) and tunneled permanent catheter (TPC) were reserved for those patients without suitable vascular anatomy for fistula creation. Vascular access failure was defined as the need for any angioplastic or surgical intervention to correct poorly or non-functioning fistulas or grafts as well as the occurrence of repeated thromboses or infections [13].

All patients provided written informed consent. They were given polysulfone dialyzer, bicarbonate dialysate (with flow of 500 ml/min) and heparin anticoagulation. Patients eligible for the study received HD 3 times per week. The blood flow was between 80–180 ml/min according to body weight. Twenty healthy children were recruited from the Pediatric Clinic of the National Research Centre to serve as controls. Clinical information, laboratory data, and a history of vascular access of the pediatric patients studied were assessed by chart review.

Clinical and Biochemical Tests

All patients were subjected to full history-taking and clinical examination. Hemoglobin (Hb), platelets (PLT), albumin (ALB), total cholesterol (TC), blood urea nitrogen (BUN), creatinine, and uric acid (UA) were measured for all patients by automatic biochemistry analyzer.

Echocardiography

Echocardiographic imaging was performed using the Vivid 3 machine (Norway) equipped with 3 and 7 MHz transducers.

Echocardiography was performed for measuring left ventricular volume indices at end systole and end diastole according to the guidelines of the American Society of Echocardiography [14].

Inflammatory Index

A peripheral blood sample was obtained prior to the hemodialysis session and immediate centrifugation was done for 10 min at 5000 rpm at 4 °C. The centrifuged serum was transferred into sterile tubes. All samples were stored at -70 °C until assay.

Serum IL-10 levels were measured by the quantitative sandwich enzyme-linked immunosorbent assay (Orgenium Laboratories, Finland) in accordance with the manufacturer's instructions [15].

High-sensitivity CRP (hs-CRP) was determined by the solid-phase chemiluminescent immunometric assay (IMMULITE/IMMULITE 1000) (supplied by SIEMENS Medical Solution Diagnostics) [16].

Excluding the possibility of HIV infection and its theoretical role in access failure was done by detection of antibodies to HIV-1 and HIV-2 using the ELISA technique (bio-ELISA, HIV- 1 + 2 (rec.) kit, Spain). The kit is a third-generation solid-phase enzyme immunoassay in which highly purified recombinant antigens are used for the combined detection of antibodies to HIV-1, HIV-2 and HIV-1 subtype O [17].

Statistical Analysis

SPSS (Statistical Package for Social Sciences) version 11.0 was used in data analysis. Data were summarized as mean \pm SD and percentage. Comparisons of continuous variables between the 2 groups were performed using the independent-sample T-Test where appropriate. One-way analysis of variance (ANOVA) was used for comparison among the 3 groups. Pearson's correlation analysis was performed to predict the associations between IL-10 and hs-CRP as well as with other numerical variables. Multiple linear regression analysis using the backward method was performed to determine the contribution of various factors as independents or covariates to hs-CRP as the dependent variable. P-value was significant at 0.05.

Table 1. Comparison of baseline characteristics among different groups

Parameter	Healthy	Patients		p
		Good access	Access failure	
Number	20	26 (65 %)	14 (35 %)	
Age (years)	10 \pm 8.80	9.57 \pm 3.71	10.96 \pm 3.46	ns
Male/Female (%)	12/8 (60 %/40 %)	19 (7) 47.5 % (17.5 %)	1 (13)* 2.5 % (32.5 %)	< 0.05* ^a
Hypertension (%)		12 (30 %)	7 (17.5 %)	ns
Cardiovascular disease		4 (10 %)	7 (17.5 %)	ns
Duration of hemodialysis (years)		2.67 \pm 1.66	2.95 \pm 1.34	ns
Duration of vascular access (years)		2.52 \pm 1.70	1.67 \pm 1.61	ns
Type of vascular access:				
AV fistula		26 (65 %)	5 (12.5 %)	
AV graft		—	5 (12.5 %)*	
TPC		—	4 (10 %)*	
Kt/V		1.71 \pm 0.41	1.63 \pm 0.34	ns
Mean fractional shortening on cardiac echo		32.83 \pm 9.60	31.20 \pm 9.95	ns

Data are means \pm SD or number (%), as applicable. Significance was estimated using the independent t-test, One-way analysis of variance (ANOVA) was used for comparison among the three groups. $P < 0.05$ was considered significant. AV: arterio-venous; TPC: tunneled permanent catheter; Kt/V: adequacy of dialysis; ns: not significant. * p value of comparing access failure group to good access group.

Results

Patient Characteristics: A Comparison of Baseline Characteristics Among Patients

The proportion of female gender was higher in the vascular access failure group ($p < 0.05$). All patients with PTEE graft and TPC were present in the vascular access failure group (group 2). The prevalences of hypertension, duration of HD, and duration of vascular access were not different between patients with or without vascular access failure (Table 1).

Hypoproteinemia (3.78 ± 0.31 vs 3.08 ± 0.21 ; $p < 0.05$) and hypercholesterolemia (209.14 ± 5.78 vs 140.30 ± 45.77 ; $p < 0.01$) were more frequent among the patients with vascular access failure (group 2) than in group 1 with good access. All patients had moderate anemia and there was no marked difference between the two groups (Table 2).

Comparison of Inflammatory Parameters Among the 3 Groups

Patients on hemodialysis produced higher levels of IL-10 than healthy controls (36.18 ± 25.55 pg/ml vs 12.70 ± 9.76 pg/ml; $p < 0.001$). Moreover, there were significantly higher serum levels of IL-10 in the vascular access failure group (group 2) than in group 1 with good access and healthy controls (45.68 ± 29.62 pg/ml vs 31.07 ± 22.01 pg/ml and 12.70 ± 9.76 pg/ml; $p < 0.05$ and $p < 0.001$, respectively) (Figure 1).

Patients with vascular access failure had significantly higher hs-CRP levels compared with group 1 and healthy controls (5.27 ± 5.44 mg/l, 2.32 ± 2.30 mg/l and 1.36 ± 0.67 mg/l; $p < 0.01$ and $p < 0.005$, respectively) (Figure 2).

Table 2. Comparison of basic biochemical data for different groups

Parameter	Good access	Access failure value
Number	26	14
Hemoglobin (g/dl)	9.83 ± 1.34	9.75 ± 1.81
WBC (10^3 /ml)	6.19 ± 1.44	6.40 ± 2.66
Platelet (10^3 /ml)	2.34 ± 65.05	231.50 ± 90.00
Albumin (g/l)	3.78 ± 0.31	$3.08 \pm 0.21^*$
Cholesterol (mg/dl)	140.30 ± 45.77	$209.14 \pm 59.78^{**}$
BUN (mg/dl)	72.23 ± 19.58	$73.00 \pm 27.95^*$
Creatinine (mg/dl)	6.18 ± 1.46	6.14 ± 1.35
Uric acid (IU/l)	6.47 ± 1.66	6.17 ± 1.17

Data are reported as means \pm SD, *p was significant if < 0.05 , **p < 0.01 , WBC: white blood cells, BUN: blood urea nitrogen

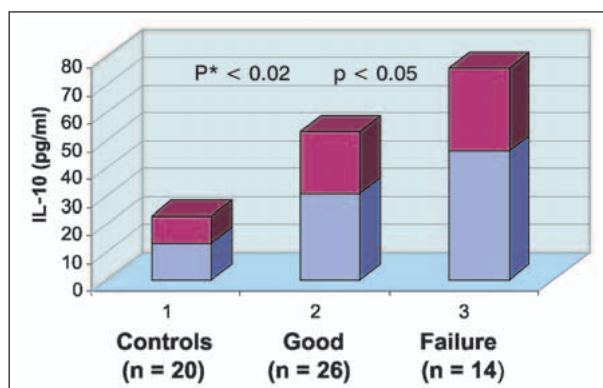


Figure 1. Comparison of the serum IL-10 levels between the good functioning group and the access failure group and in healthy controls. Columns represent mean \pm SD. *p value of comparing good to controls

All HD patients were sero-negative for antibodies of both HIV-1 and HIV-2.

Correlation Between hs-CRP and IL-10 Levels

The increase of hs-CRP values negatively correlated with serum levels IL-10 in HD patients, ($r = -0.36$; $p = 0.01$) (Table 3).

Comparisons of IL-10 Levels and CRP Value with Different Variables in HD Patients

The increase of hs-CRP levels was negatively related to vascular access duration ($r = -0.35$; $p = 0.02$), serum albumin ($r = -0.78$; $p = 0.04$), serum cholesterol ($r = -0.36$; $p = 0.002$), and fractional shortening (FS%) on cardiac echo ($r = -0.36$; $p = 0.01$). Weak inverse correlation was found between serum IL-10 and vascular access duration ($r = -0.37$; $p = 0.09$) (Table 4).

On multiple regression analysis, the presences of a PTEE graft ($\beta = 0.44$; $p = 0.05$) or TPC ($\beta = 0.37$; $p = 0.05$), cardiovascular disease ($\beta = 0.06$; $p = 0.009$), vascular access duration ($\beta = 0.37$; $p = 0.09$) and WBCs ($\beta = 0.44$; $p = 0.08$) were independent predictors of elevated CRP in HD patients (Table 5).

Discussion

Arteriovenous access failure is multifactorial in nature with contributions from both medical and surgical etiologies. Most medical causes are derived from Virchow's triad of endothelial cell injury, stasis, and microinflammation [18]. The present study provides up-to-date insight into microinflammation and VA dysfunction. An aberrant wound-healing process in response to chemical or mechanical injury is believed to explain the pathophysiology of NIH; VSMC proliferates and migrates into the intima of vessels, where they induce intimal expansion via extracellular matrix deposition [18].

Table 3. Correlation between interleukin-10 and hs-CRP in HD patients

Parameter	Interleukin-10	
	r	p
High-sensitivity C-reactive protein	-0.36	0.01*

Correlation was performed by Pearson's analysis. Significant at *p < 0.05 .

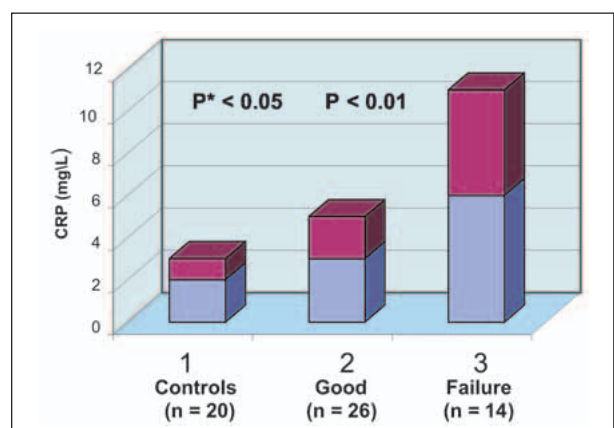


Figure 2. Comparison of the serum hs-CRP levels between the good functioning group and the access failure group and in healthy controls. Columns represent mean \pm SD. *p value of comparing good to controls

Table 4. Correlation of interleukin-10 and hs-CRP with different variables in HD patients

Parameter	IL-10		hs-CRP	
	r	p	r	p
Age	0.14	ns	-0.09	ns
Vascular access duration	-0.37	0.09	-0.35	0.02*
KT/V	0.17	ns	0.05	ns
Albumin	0.05	ns	-0.78	0.04*
Hb %	-0.23	ns	-0.09	ns
Cholesterol	0.14	ns	-0.91	0.002**
FS %	-0.04	ns	-0.36	0.01*

Correlation was performed by Pearson's analysis. Significant at * $p < 0.05$ or ** $p < 0.01$, hs-CRP: high-sensitivity C-reactive protein; KT/V: adequacy of dialysis; Hb: hemoglobin; FS %: fractional shortening; ns: not significant

This study showed that female gender, hypoproteinemia, and hypercholesterolemia were associated with vascular access failure. This is in agreement with previous reports [19, 20]. Female patients may have vessels of a smaller diameter. Hernandez et al [19] reported that female gender appears to be an independent risk factor for early failure of AVF when adjusted for initial artery diameter. Hypoproteinemia that results in part from inflammation might be related to vascular access failure. Inflammation decreases the synthesis of protein in the liver and is associated with a greater fractional catabolic rate and, when extreme, increases the transfer of albumin out of the vascular compartment. A vicious cascade of events ensues in which inflammation induces anorexia and reduces the effective use of dietary protein and energy intake and augments the catabolism of protein. A previous study [13] found a lower graft patency in patients with hypoproteinemia. De Marchi et al [20] reported that a high total cholesterol/HDL cholesterol ratio and hypertriglyceridemia are powerful risk indicators for fistula obstruction of patients on hemodialysis.

The present study showed that serum IL-10 levels were much higher in the vascular access failure group compared to the good functioning access group. Sung et al [13] reported that it is not clear whether the fibro-proliferative response occurs by way of inflammatory pathways or whether the inflammation is secondary to another deriving mechanism, several studies have suggested that inflammatory cytokines play a critical role in NIH. TNF- α , a proximal inflammatory cytokine, stimulates the expression of adhesion molecules and other pro-inflammatory cytokines including platelet-derived growth factor (PDGF) and transforming growth factor- β 1 (TGF- β 1), which are important mediators of VSMC proliferation and migration [21]. Previous studies observed elevated levels of IL-10 [1, 2, 13], and the substance was proven to be effective in these patients, as well. Nevertheless, higher levels of IL-10 are needed for comparison with healthy persons to limit the strong inflammatory activation of ESRD patients. In light of these findings, the elevation of IL-10 seems to be a counter-regulatory mechanism to control uremia- and dialysis-induced activation of inflammation. IL-10 exerts anti-inflammatory activities directed against the function of inflammatory cells, and inhibits the production of inflammatory cytokines, such as TNF- α , IL-1, and IL-8. IL-10 was shown to interfere with NIH, after balloon injury or stent implantation, and potentially abrogates the proliferative response to atherogenic mitogens [22, 23].

The critical role of TNF- α and IL-10 in NIH suggests a relationship between TNF- α and IL-10 levels and vascular access failure in patients on HD [13]. This suggests that inflammation, especially activation of vascular inflammatory cytokines, might be an important factor in mediating the VA dysfunction. This result is in agreement with Sung et al [13],

Table 5. Multiple linear regression analysis between hs-CRP and different variables

Parameter	β	p
Cardiovascular disease	0.62	0.009**
Type of vascular access:		
– arteriovenous graft	0.44	0.05*
– tunneled permanent catheter	0.45	0.05*
Vascular access duration	0.37	0.09
WBC	0.44	0.08

* $p < 0.05$ or ** $p < 0.01$ was considered significant. WBC: white blood cells

who found that IL-10 levels were higher in patients on HD than in healthy controls, but no significant difference was revealed among the patients with or without access failure. They reported that an altered immune response and inflammation might contribute to vascular access failure.

Our study showed that serum hs-CRP levels were significantly higher in HD patients with vascular access failure compared to the good functional access patients and to healthy controls. It is well known that AVF is one of the most important factors and plays a vital role in hemodialysis patients. VA dysfunction has been a major obstacle to induce the technique failure and brings about high morbidity and hospitalization rates. Studies have found that thrombosis and vascular intimal hyperplasia are the main reason for VA dysfunction [24, 25]. However, the exact mechanism has not been fully elucidated yet. Sukhatme et al [26] put forward that endothelial injury, immune/inflammatory responses, and hemodynamic effects may contribute to the initiation of vascular intimal hyperplasia. Among them, microinflammation has raised increasing attention.

Microinflammation is a state in which serum CRP rises but does not exceed 10–15 mg/l [27]. Accumulating evidence suggests that ESRD is a state of chronic microinflammation. Lately, increasing research has shown that inflammatory mediators such as CRP are closely linked with the prevalence of cardiovascular disease and survival rates in patients with ESRD [28].

Is microinflammation linked to hyperplasia of an internal fistula intima? Several observations support a hypothesis that inflammatory cytokines and growth factors induced by CRP may stimulate smooth muscle cell proliferation and increase the production of extra-cellular matrices [29–31]. Specifically, the disorder of the endothelium may further stimulate intimal hyperplasia, atherosclerosis, which finally contributes to thrombosis and stenosis of VA [32]. In response to vascular injury, smooth muscle cells exhibit many changes that ultimately result in the pivotal processes of proliferation, migration, and apoptosis. The smooth muscle cell is thought to undergo a phenotypic change characterized by changes in affinity of smooth muscle cell integrins for their ligands, expression of adhesion molecules, production of numerous cytokines, and growth factors including IL-1 and TNF- α . This phenotypic switch results in the synthesis of more cytokines and growth factors that act as paracrine mediators to activate other smooth muscle cells, facilitating leukocyte chemotaxis and infiltration into the vessel wall, and stimulation of extra-cellular matrix components such as collagen, elastin, and proteoglycans. Activated smooth muscle cells also proliferate and migrate into the vascular intima, where the inflammatory milieu promoting the maintenance of the activated state with continued production of cytokines, growth factors, and extracellular matrices, ultimately contributing to the development of hyperplasia of the intima [8, 33].

This study showed a negative correlation between IL-10 levels and hs-CRP values. This finding indicates that there is

a uremia-associated immune defect that can be explained by the IL-10-CRP axis [34]. Unstable atherosclerotic disease is related to systemic inflammation. While this inflammation remains at a subclinical level in otherwise healthy individuals, chronic elevation of pro-inflammatory cytokines is a common feature in patients with ESRD. Current hypotheses on the pathogenetic links between inflammation and atherosclerosis emphasize that cytokine-producing monocytes/macrophages can actively infiltrate atherosclerotic plaques. A high activation level of this cell type may contribute to plaque growth [34].

In the healthy, some 15–20 % of circulating monocytes may be activated for cytokine production. This percentage is much higher in dialysis patients (50 %), which may contribute to the rapid progression of atherosclerosis. Anti-inflammatory mechanisms such as IL-10 limit the production of a broad range of pro-inflammatory factors. Animal models, as well as clinical findings, suggest an involvement of this cytokine in the pathogenesis of vascular lesions. In HD patients, a protective role of IL-10 against systemic inflammation could be proven [34]. A high interindividual variability in IL-10 production leads to distinct patient groups who can or cannot effectively limit the uremia- and dialysis-induced inflammation. IL-10 levels strongly influence the range of variation of CRP, the most widely used marker of inflammation in dialysis patients [34]. The decrease or absence of IL-10 favors the development of atheromatous lesions with signs characteristic for increased microinflammation, vulnerability and thrombosis. IL-10 inhibits many cellular processes that could play an important role in plaque progression, rupture and thrombosis. This result is in accordance with Seyrek et al [34], who found an inverse correlation between CRP and IL-10 levels in HD patients. They concluded that the limitation of the anti-inflammatory response in atherosclerotic uremic patients is a triggering or contributory factor for atherosclerosis and thrombosis.

Girnatt et al [35] reported that the balance between inflammatory markers and anti-inflammatory cytokines is a major determinant of outcome. However, the present study represents a small and observational study, it was beyond the scope of the study to assess the relationship between IL-10 and CRP and patients' outcome.

Our present study revealed an inverse correlation between hs-CRP levels and serum albumin. Malnutrition and inflammation are associated with ESRD. Inflammation leads to reduced synthesis of albumin, transferrin and other proteins and increases their catabolic rates. This result is in agreement with Pekovic et al [36], who found an inverse correlation between serum albumin and inflammatory markers and reported that the decrease of nutritional parameters in HD patients was related to the degree of inflammation. Blake and Ridker [7] reported that increased hs-CRP levels and reduced serum albumin are early predictors of inflammation in both renal and non-renal disease.

Inverse correlations were detected between hs-CRP levels and both serum cholesterol levels and fractional shortening percentage as parameters for vascular atherosclerosis and thrombosis. Markers of inflammation such as CRP powerfully predict the cardiovascular disease in hemodialysis patients as well as progression of vascular injury [26, 37]. Furthermore, elevation of serum CRP and cholesterol levels predict mortality in this population and they are risk factors for cardiovascular disease, both in the general and ESRD population [38]. It has been well-documented that CRP is not only a marker of an underlying inflammatory atherosclerotic process, but also the inducer of atherosclerosis and inflammation [29, 30].

The present study did not reveal any correlations between serum IL-10 levels and any of the vascular access failure markers such as age, serum cholesterol, serum albumin, and fractional shortening percentage except for a weak correlation with vascular access duration. These negative results should not be interpreted as an argument against the importance of inflammatory responses elicited in vascular access failure and the critical role of IL-10 as a regulator. Instead, apparent lack of association may reflect the complexity of interactions underlying the NIH and subsequent vascular stenosis, and may also largely be attributable to the inadequate sample size available for our study. We did not compare the diameter of the access vessels, an important factor for the development of vascular access failure [19]. A relationship between IL-10 levels with inflammatory disease was not always revealed. A relationship was not demonstrated in coronary artery restenosis after angioplasty [39], rheumatoid arthritis, and chronic hepatitis [40, 17], development of cervical cancer [41], and prognosis of lymphoma and breast cancer [42, 43].

In this study, the presences of AVG or TPC, cardiovascular disease, vascular access duration, and WBC were independent predictors for increased hs-CRP levels. Arterio-venous grafts and tunneled permanent catheters are increasingly being used in HD patients. However, their role in baseline inflammatory status has not been fully evaluated. AVG and TPC have a higher degree of chronic inflammation than AVF [44]. Adriana et al [45] reported that the presence of a catheter is an independent determinant of an exaggerated inflammatory response in chronic HD and represents a potentially modifiable risk factor.

Conclusion

This study showed that female gender, hypoproteinemia, and hypercholesterolemia could be risk factors for the development of access failure. Patients with VA dysfunction have significantly higher levels of serum IL-10 and hs-CRP. The imbalance of inflammatory markers and anti-inflammatory cytokines could have influenced the development of access failure. These impressive data suggest that microinflammation might be involved in the development of VA dysfunction. Moreover, the presence of AVG and TPC closely correlates to hs-CRP levels.

Recommendations

1. In view of the importance of VA in the maintenance HD, it is highly worthwhile to further investigate the exact mechanism of micro-inflammation in vascular intimal hyperplasia, which generates a novel strategy to prolong the survival of VA and improve the outcome of HD patients.
2. Patients having risk factors for vascular access failure, especially if more than one, deserve to receive a tailored prescription, e.g. older children treated for persistent hypercholesterolemia with statins.
3. A further large study population should follow to identify markers that are useful in the detection of risk factors for access failure to improve management of HD patients.

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