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Biochemical Risk Factors Associated with Arteriovenous Fistula Failure in Hemodialysis Patients

Mohamed A. Elsamnoudy, Abdallah A. Elsawy, Mohammed M. Dawoud and Kamal M. Okasha

Department of Internal Medicine, Faculty of Medicine, Tanta University, Tanta, Egypt

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ABSTRACT

Background: Hemodialysis is the most common method of renal replacement therapy for end stage renal disease (ESRD) patients and the AVF is the best vascular access of choice for hemodialysis as recommended by KIDGO. AVF failure is the leading cause of morbidity and mortality for emodialysis patients. It is a challenging process in which improvement of outcome of the AVF will improve quality of life of hemodialysis patients and minimize health care resources and costs related to vascular access dysfunction. **Objective**: This study shows the risk factors contributing to AVF dysfunction in order to find out some preventive measures to decrease the rate of AVF failure. **Patients and methods:** 300 patients with ESRD were divided into 2 groups: control group: 200 patients with functioning AVF. Case group: 100 patients with AVF dysfunction. All patients included in the study were subjected to laboratory investigations (CBC, blood urea and serum creatinine, cholesterol, triglycerides, HbA1C, serum albumin, Ca, Po4, PTH, PT, INR, CRP & ESR) and imaging in the form of Doppler ultrasound of the AVF. **Results:** Our study results show a significant relation between arterio-venous access and some risk factors as low hemoglobin level, high platelet count, high renal functions, dyslipidemia, hypoalbuminemia, and elevated CRP & ESR denoting the presence of inflammation. **Conclusion:** the most independent risk factors for AVF dysfunction were anemia, dyslipidemia, high platelets, high renal functions, hypoalbuminemia and elevated ESR & CRP.

Keywords: Chronic kidney disease, Hemodialysis, AVF & risk factors,

1. Introduction

Chronic kidney disease (CKD) is a major health problem worldwide with a rapidly growing incidence in the last decade (Xie *et al.,* 2018). By the influence of global aging, the number of CKD patients who progress to end-stage renal disease (ESRD) which is the last stage of chronic kidney disease is markedly raising which in turn increases the demand for renal replacement therapy (RRT) (Donca *et al.,* 2012). Hemodialysis (HD) is the most common method of RRT. Due to its fewer complications, it has become a widely safe and well-tolerated therapy for ESRD patients. It requires vascular access for dialysis such as central venous catheters (CVC), arteriovenous graft (AVG), and arteriovenous fistula (AVF) (Ghonemy *et al.,* 2016). The Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines recommend autologous AVF as the vascular access of choice in hemodialysis and the preferred site is the wrist, preferably in the non-dependant arm regarding the higher quality of life, the best patency rate, requiring lowest re-intervention rate, and having lower complication rates (Sarioglu *et al.,* 2020). Despite the advantages of AVF rather than other vascular accesses, AVF dysfunction particularly early and late failure represents one of the most important causes of morbidity and mortality in hemodialysis patients, attributing to up to 20% of all hospitalizations related to AV access problems in western countries and consuming a significant amount of the health care costs (Gameiro and Ibeas, 2020). Thrombosis is considered a leading cause of AVF failure and usually results from stenotic lesions in the venous outflow system. The main underlying pathology of

Corresponding Author: Mohamed A. A. Elsamnoudy, Department of Internal Medicine, Faculty of Medicine, Tanta University, Tanta, Egypt. E-mail: elsamnoudymohamed93@gmail .com

AVF failure is neo-intimal hyperplesia which progresses to stenosis with subsequent thrombosis. The exact mechanism of neo-intimal hyperplasia is still unknown (MacRae *et al.,* 2016). However, inflammation and atherosclerosis have been implicated in the pathogenesis of intimal hyperplasia (Roy-Chaudhury *et al.,* 2014). There are many risk factors precipitate AVF dysfunction including clinical factors such as advanced age, female gender, uncontrolled DM, and history of cardiovascular diseases, surgical factors that depend on the surgeon, surgical procedures, and post-operative care, other laboratory factors which include low Hb level, high platelets, hypercholesterolemia, hypoalbuminemia, high urea, and inflammatory markers as CRP and ESR which denote the presence of inflammation (Kaygin *et al.,* 2013). In our study we focus on risk factors associated with AVF failure and their impact on the pathogenesis of early and late AVF failure in order to find out some preventive measures to decrease the rate of access failure so we can improve life expectancy of HD patients and decrease health care resources and costs related to vascular access dysfunction.

2. Patients and Methods

This study is a cross sectional one including 300 patients with ESRD divided into 2 groups: **Control group**: 200 patients with functioning AVF. **Case group**: 100 patients with AVF dysfunction. All patients were subjected to full history taking, general examination, local examination of the fistula, laboratory investigations (CBC, blood urea and serum creatinine, cholesterol, triglycerides, HbA1C, serum albumin, Ca, Po4, PTH, PT, INR, CRP & ESR) and imaging in the form of Doppler ultrasound of the AVF. The following are the inclusion and exclusion criteria of our study:

The inclusion criteria included Adult chronic renal failure patients on regular HD using AV access for more than 18 years old.

The exclusion criteria included Patients with a previous history of AV access dysfunction, Pediatric patients on regular HD, Patients on HD by other methods rather than AV access, and patients unwilling to participate in the study.

Provision of privacy: Privacy of all patient's data was guaranteed by a special code number for every patient's file that includes all his or her investigations.

Data collection:

All the participants in the study were subjected to:

Consent: Permission was obtained from Research Ethics Committee as a part of the Quality Assurance Unit in the Faculty of Medicine at Tanta University to conduct this study and to use the facilities in the hospital. Informed written consent was obtained from all patients after a full explanation of the benefits and risks of the study.

History taking: Including age, sex, past medical history, any previous medical treatment if present, period of HD, past access related dysfunction, and duration of vascular access.

Clinical examination: Measurement of systolic and diastolic blood pressure. Head, neck, chest, cardiac and abdominal examination to exclude subjects with any abnormal findings.

Full AVF examination:

Through inspection, palpation, and auscultation of AVF

Inspection if there are any abnormalities of fistula present or not as swelling, scars discoloration or erosions of skin, or prominent veins.

Palpation of fistula if tender or not, pulsatile or not, thrill present or absent.

Auscultation of the bruit that is continuous in normal AVF during systole and diastole.

Lab investigation: including complete blood picture, C reactive protein and ESR, lipid profile (cholesterol and triglycerides), serum urea and creatinine, calcium, phosphorous, parathyroid hormone, Serum albumin, PT, INR, PTT, and HbA1c.

Statistical analysis:

Data were analyzed using the IBM® SPSS statistical software, version 21. Qualitative data were described using numbers and percentages. The Kolmogorov Smirnov test was used to verify the normality of distribution. Quantitative data were described using range (minimum and maximum), mean, standard deviation, and median. Chi-squared test was used for comparing the qualitative data and when it was inappropriate it was replaced by the Monte Carlo test. A student t-test was used to compare the two means in different groups. Linear correlation analysis was done by Spearman coefficient correlation and used to test the positive or negative associations between different variables. For the risk estimated, linear regression was used to detect the predictor variables. The level of significance was adopted at $p<0.05$ and statistically highly significant at $P \leq 0.001$.

3. Results

The present study was conducted on 300 ESRD patients on maintenance hemodialysis using AVF divided in 2 groups: **Group 1** included 100 cases of AVF dysfunction and **Group 2** included 200 cases of functioning AVF as control group. The patients were recruited from Tanta University hemodialysis units in the period of June 2021 to June 2022. The patient laboratory and radiological data were recorded in a special observation sheet. The results were assessed as follow:

There was statistically significant decrease between group A and group B as regard hemoglobin, and platelet count (p-value ≤ 0.05) (Table 1).

According renal functions, there was statistically significant increase between group A and group B as regards urea and creatinine (p-value ≤ 0.05) (Table 2).

In our study, there is an association between arteriovenous access dysfunction and high HbA1c which ranges from 5 to 15 with a mean ± SD of 7.44±2.06 (Table 3).

There was statistically significant increase between group A and group B as regards cholesterol and triglycerides (p-value ≤ 0.05) (Table 4).

Our results show statistically significant decrease between group A and group B as regard albumin (p-value ≤ 0.05) (Table 5).

Finally, regarding inflammatory markers such as ESR 1hour, ESR 2hour, and CRP, there was statistically significant decrease between group A and group B as regards ESR 1hour, ESR 2hour, and CRP (p-value ≤ 0.05) (Table 6).

Patients with arteriovenous access dysfunction and patients with functioning arteriovenous access groups were negatively correlated with platelets, urea, creatinine, triglycerides, cholesterol, HBA1C, ESR 1hour, and ESR 2hour (Table 7).

Also, patients with arteriovenous access dysfunction and patients with functioning arteriovenous access groups were positively correlated with albumin and CRP (Table 8).

The regression analysis revealed that anemia, platelets, urea, creatinine, triglycerides, cholesterol, albumin, ESR 1hour, and CRP were significantly associated with affecting patients with arteriovenous access dysfunction and patients with functioning arteriovenous access (Table 9).

Table 1: Complete blood picture (CBC) among the studied groups.

Groups / Parameters	Group A (n=100) (33.33%)	Group B (n=200) (66.66%)	Test of sig.	P-Value
Hemoglobin (g/dL)				
Mean ± SD	9.199±1.41	9.707±2.71	t= -2.126	**0.034*(a)**
Min.–Max.	4 – 11.5	4.3 – 16.3		
Platelets (10^3/mm3)				
Median (IQR)	310.5 (200)	219.3(169)	H= 5609.5	**0.000**(C)**
Min.–Max.	92 – 756	44 -571		
Min.–Max.	3.2 – 22.6	1.9 – 18.3		

Table 2: Kidney function tests among the studied groups.

Groups / Parameters	Group A (n=100) (33.33%)	Group B (n=200) (66.66%)	Test of sig.	P-Value
Urea (mg/dL)				
Median (IQR)	58 (43)	44 (133)	H= 8388	**0.023*(c)**
Min.–Max.	33 – 260	12 – 361		
Creatinine (mg/dL)				
Median (IQR)	4.15 (1.5)	3.5 (2.2)	H= 7003	**0.000**(c)**
Min.–Max.	2.4 – 7.4	0.6 – 9.2		

Table 3: HBA1C among the studied groups.

Groups / Parameters	Group A (n=100) (33.33%)	Group B (n=200) (66.66%)	Test of sig.	P-Value
HBA1C (%)				
Mean ± SD	7.44±2.06	6.90±2.01	t= 2.173	**0.031*(a)**
Min.–Max.	5 – 15	4.5 – 12.5		

Table 4: Lipid profile among the studied groups.

Groups / Parameters	Group A (n=100) (33.33%)	Group B (n=200) (66.66%)	Test of sig.	P-Value
Cholesterol (mg/dL)				
Mean ± SD	227.64±94.85	180.61±45.22	t= 4.698	**0.000**(a)**
Min.–Max.	145 – 759	115 – 534		
Triglycerides (mg/dL)				
Mean ± SD	169.88±41.59	135.95±41.16	t= 6.707	**0.000**(a)**
Min.–Max.	103 – 360	68 – 287		

Table 5: Statically analysis of albumin among the studied groups.

Groups / Parameters	Group A (n=100) (33.33%)	Group B (n=200) (66.66%)	Test of sig.	P-Value
Albumin (g/dL)				
Mean ± SD	3.36±0.76	3.66±0.69	t= -3.253	**0.001**(a)**
Min.–Max.	1.2 – 4.7	1.5 – 4.8		

Table 6: Statically analysis of erythrocytes sedimentation rate (ESR) & C-reactive protein (CRP) among the studied groups.

Groups / Parameters	Group A (n=100) (33.33%)	Group B (n=200) (66.66%)	Test of sig.	P-Value
ESR (1 hour) (mm/hr)				
Mean ± SD	30.66±10.71	24.24±10.22	t= 5.042	**0.000**(a)**
Min.–Max.	13 – 56	7 - 47		
ESR (2 hour) (mm/hr)				
Mean ± SD	59.98±22.46	49.12±21.57	t= 4.053	**0.000**(a)**
Min.–Max.	22 – 102	12 - 98		
CRP (mg/L)				
Median (IQR)	6 (11)	8 (21)	H= 7373	**0.000**(c)**
Min.–Max.	1 – 96	2 - 118		

Table 7: Spearman correlation of patients with arteriovenous access dysfunction and patients with functioning arteriovenous access with other parameters.

Variables	Patients with arteriovenous access dysfunction and patients with functioning arteriovenous access	
	r	p
Hemoglobin	0.069	0.236
Platelets	**-0.358**	**0.000****
Urea	**-0.132**	**0.023***
Creatinine	**-0.245**	**0.000****
HBA1C	**-0.161**	**0.005***
Triglycerides	-0.424	**0.000****
Cholesterol	**-0.332**	**0.000****
Albumin	**0.203**	**0.000****
ESR1hour	**-0.264**	**0.000****
ESR2hour	**-0.227**	**0.000****
CRP	**0.215**	**0.000****

*: Statistically significant at $p \leq 0.05$, **: Statistically significant at $p \leq 0.001$

Table 8: Logistic regression for predictor factors affecting patients with arteriovenous access dysfunction and patients with functioning arteriovenous access.

Independent variables	Odds Ratio (95%) CI	P- value
Hemoglobin	0.926 (0.675 – 1.270)	0.632
Platelets	0.991 (0.986 – 0.996)	**0.000****
Urea	1.063 (1.036 – 1.090)	**0.000****
Creatinine	0.305 (0.165 – 0.564)	**0.000****
HBA1C	0.601 (0.330 – 1.094)	0.096
Triglycerides	0.959 (0.938 – 0.980)	**0.000****
Cholesterol	0.967 (0.950 – 0.985)	**0.000****
Albumin	2.427 (1.071 – 5.500)	**0.034***
ESR 1hour	0.791 (0.654 – 0.957)	**0.016***
ESR 2hour	1.076 (0.989 – 1.170)	0.087
CRP	1.114 (1.047 – 1.185)	**0.001****

*: Statistically significant at $p \leq 0.05$**: Statistically significant at $p \leq 0.001$

Table 9: Receiver operating characteristic (ROC) curves analysis of urea, creatinine, total calcium, phosphorus, hemoglobin, parathyroid hormone, albumin and CRP in patients with arteriovenous access dysfunction and patients with functioning arteriovenous access.

Parameters	AUC	p	95% C.I	Cut off	Sensitivity	Specificity	PPV	NPV
Urea	0.581	**0.023***	(0.517 – 644)	43.5	81%	52%	45.75%	84.55%
Creatinine	0.650	**0.000****	(0.589 – 0.711)	3.22	83%	57%	49.11%	87.02%
Hemoglobin	0.542	0.235	(0.394 – 0.522)	8.75	66%	59%	44.59%	77.63%
HBA1C	0.598	**0.005***	(0.533 – 0.664)	5.85	75%	57.5%	46.87%	82.14%
Albumin	0.624	**0.000****	(0.555 – 0.694)	3.05	81.5%	65%	82.32%	63.72%
CRP	0.631	**0.000****	(0.564 – 0.698)	5.5	80.5%	63%	81.31%	61.76%

AUC: Area Under a Curve. p value: Probability value.
CI: Confidence Intervals. NPV: Negative predictive value.
PPV: Positive predictive value. CRP: C-reactive protein.
*: Statistically significant at $p \leq 0.05$, **: Statistically significant at $p \leq 0.001$

4. Discussion

Chronic Kidney disease is a common serious health problem with expected rising incidence and prevalence worldwide especially among countries with low and middle incomes (Grans *et al.,* 2020).

Hemodialysis is considered the most common way for renal replacement therapy that is required for CKD patients who develop to end-stage renal disease (Ren *et al.,* 2018).

The arteriovenous fistula is considered the best choice for the vascular access required for patients on regular HD, because it has the best patency, requires the fewest interventions, and has the least complications as regards other access types (Amadis *et al.,* 2020).

The most concerning complication with AVF is access failure which results mainly from fistula stenosis and thrombosis. AVF dysfunction is considered a huge clinical problem nowadays with significant clinical morbidity, mortality, and economic burden within the ESRD population (Roy-Chaudhury *et al.,* 2006).

There are many risk factors associated with AVF dysfunction as old age, uncontrolled DM, and hypercholesterolemia (Roy-Chaudhury *et al.,* 2006).

The aim of our study is to describe the pathogenesis of AVF failure and provide a comprehensive analysis of the associated risk factors and causes of AVF failure, in order to reach possible future preventive and therapeutic methods.

The present study was conducted on three hundred subjects (159 male and 141 female), aged from 19 to 93, diagnosed with end-stage renal disease depending on HD, and divided into 2 groups:
Group I: includes 100 HD patients with AVF dysfunction.
Group II (control group): includes 200 HD volunteers with functioning AVF.

The patients were recruited from Tanta University hemodialysis units in the period between," June 2021 to June 2022 ".

In our study, there are two remarkable changes in the CBC picture. First, decreased HB level (anemia) is found. It ranges from 4 to 11.5 mainly around 8. Anemia plays a significant role in AVF dysfunction. That is related to the association of anemia with inflammatory states and the presence of co-morbidities in many HD patients. Also, anemia is manifested by pallor so HD patients at high risk of access dysfunction appear to be more pallor than the others.

This result is in line with the result of Zadeh et al., (2008) Prospective observational data were analyzed from a non-randomized sample (n=100) of HD patients using AVF. It reported that anemia (HB <8 g/dl) was associated with AVF primary failure (Zadeh *et al.,* 2008).

Also, our result is in agreement with Hara *et al.* (2020) a longitudinal cohort study sought to confirm the effects of malnutrition, inflammation, and anemia on VA failure. We included 177 patients with CKD with first-time arteriovenous fistulas. It demonstrated that malnutrition, inflammation, and anemia independently and synergistically predispose to VA failure.

The second change in the CBC picture found in our study results and related to the risk of AVF failure is an elevated number of platelets. That could be explained as the main pathophysiology underlying neointimal hyperplasia and atherosclerosis is inflammation and Platelets play a significant role in both prothrombotic and proinflammatory events by contacting with endothelium and inducing cytokine secretion. Neointimal hyperplasia is the main reason for AVF stenosis and thrombosis.

This is compatible with the result of Sarioglu *et al.,* (2020) a retrospective study carried on 95 patients with arteriovenous fistula dysfunction. It showed that high platelet count was found to be significantly associated with AVF dysfunction.

In contrast to our study results, Memetoglu *et al.* (2015) a retrospective cohort study including 313 patients who underwent primary AVF creation procedures for hemodialysis. It stated that the failure rate was not significantly related to the parameters of HB and platelets.

The study results show the association between the rate of AVF failure and the raised levels of renal function (urea and creatinine). It could be explained as Uremic toxins are known to increase oxidative stress, endothelial dysfunction, intima-media thickness, and calcification in the vasculature leading to early failure.

This is in agreement with the result of Aitken *et al.* (2014) a retrospective analysis of a prospectively collected database of 569 simple arteriovenous fistulae {radiocephalic (RCF) and brachiocephalic (BCF)} created in our tertiary referral vascular access center during a three-year period. It illustrated that increasing serum urea was associated with worse clinical patency at 6 weeks and poorer long-term outcomes from RCF. Similarly, in those patients who had already commenced HD at

the time of access creation, dialysis on the same day as surgery was associated with better early patency rates.

On the other hand, Duque *et al.* (2017) a retrospective study on 612 patients who underwent AVF creation between 2003 and 2015 at the University of Miami Hospital and Jackson Memorial

Hospital. It revealed no association between blood urea level and serum creatinine level with AVF maturation and early failure. In our study, there is an association between arteriovenous access dysfunction and high HbA1c which ranges from 5 to 15 with a mean ± SD of 7.44±2.06.

This result matches the result of Wärme *et al.* (2021) a retrospective observational study included 153 chronic HD patients (Cases) referred to a total of 473 radiological investigations due to clinically suspected complications of their native AVF. Another group of chronic HD patients ($n = 52$) who had a native AVF but were without history of previous complications for at least 2 years were controls. It showed a higher level of HbA1c among cases of access dysfunction. High HbA1c indicates a worse metabolic control. Such metabolic disturbance may impair the vascular endothelium which reflected the risk of dysfunction with elevated HbA1c.

In contrast to our result, Keser *et al.* (2021) a retrospective cohort study including 127 newly created AVFs in 117 patients (67 males, 50 females) who underwent primary AVF operation. It reported that there was no significant correlation between HbA1c levels and primary AVF failure (p=0.406). The ROC curve analysis established no cut-off value of HbA1c level to predict primary AVF failure. That may be explained by some theories. It has been reported by many authors that the correlation between HbA1c and blood glucose is impaired in CKD patients so HbA1c may not be a reliable indicator of blood glucose control in these patients. Also, reduced red blood cell survival and the common use of erythropoietin-stimulating agents increase the rate of young erythrocytes in these patients. These erythrocytes have less exposure time to glucose, which affects HbA1c levels. Several studies have indicated that the measured HbA1c levels of diabetic CKD patients are lower than indicated by their blood glucose levels, and thus HbA1c level mispresents glycemic control so it may be misleading to assess HbA1c as an accurate predictor of blood glucose control in CKD patients despite hyperglycemia seems to be an essential parameter affecting AVF failure.

According to our demographic data, hypercholesterolemia and hypertriglyceridemia are risk factors of AVF failure as they cause vascular endothelial damage.

Our result agrees with the result of Li *et al.* (2021) a retrospectively study conducted on One hundred and twenty-one patients who underwent anastomosis for AVF. Seventy-seven patients satisfied the inclusion criteria and were included in the final analyses. Patients were divided into two groups based on the function of vascular access.

There were significant differences in total cholesterol (TC) and low density lipoprotein (LDL) levels between patency and dysfunction group ($P<0.05$) of AVFs denoting that hypercholesterolemia are independent risk factors for primary AVF dysfunction in patients with MHD. In brief, the mechanism of action could be formation of atheromatous plaques and atherosclerosis which lead to disruptions in the vascular endothelium, enabling platelet accumulation on the endothelium and initiating clotting. Many authors recommend statin use as prophylaxis against AVF failure by its endothelium-protective effects besides their lipid-lowering ability.

In contrast to our result, Zeid *et al.* (2015) a cross section study carried on 40 patients divided into 2 groups, group I contain 20 patients with thrombosed AVF proved by Doppler ultrasound and group II 20 patients with normally function AVF for at least 6 months with no previous vascular access thrombosis. It demonstrated no statistical significant differences between the 2 groups regarding total cholesterol, LDL-cholesterol, HDL-cholesterol, VLDL-cholesterol and TGs.

Kirkpantur *et al.* (2008) a retrospective cohort study in which 99 maintenance hemodialysis patients were reviewed for 3 years. It reported that patients with AVF thrombosis and patent AVF had similar serum levels of total cholesterol and triglyceride levels. However, lipid sub-fractions (LDL-C and HDL-C) were associated with AVF thrombosis, despite that TC is the sum of LDLC and HDL-C levels based on the Friedewald equation. Low LDL-C could predispose to AVF dysfunction as AVF stenosis accounts for most of the cases of AVF thrombosis and is histologically characterized by intimal hyperplasia induced by growth factors, among which transforming growth factor- 1 (TGF- 1). LDL-C has been shown to suppress TGF- responsiveness by increasing lipid raft or facilitate rapid degradation of TGF- and thus suppress TGF- -induced signaling. Low HDL-C levels were related to an increased risk of AVF thrombosis among maintenance hemodialysis patients as HDL-C serves as antioxidant and

reduces the oxidized LDL-C. Furthermore, HDL-C decreases the cytokine-induced expression of the adhesion molecules by vascular endothelial cells. In conclusion, Serum levels of lipid sub-fractions are associated with AVF thrombosis in maintenance hemodialysis patients despite of normal TC level.

Our study results also show significant relationship between hypoalbuminemia and AVF dysfunction.

This is in line with Tanaka *et al.* (2016) a retrospective study included patients who had VA (arteriovenous fistula or graft) created between May 2010 and July 2016 about 913 VA creations were performed among 804 patients. Serum albumin level was significantly lower in the early VA failure group than in the without early failure group so low albumin level was associated with early VA failure. The role of hypoalbuminemia in AVF failure could be explained as low serum albumin cause reduction in the oncotic pressure and the blood flow rate post-AVF creation and hemodialysis as compared to individuals with normal serum levels leading to decreased in the effective circulatory volume (ECV). Reduction in both oncotic pressure and ECV lead to subsequent decrease of cardiac output. Another function of albumin is platelet function inhibition and antithrombotic effect, meaning that those patients with low albumin may be exposed to fistulae failure due to an increased risk of thrombosis exacerbated by low flow state (reduced cardiac output). Also, low albumin is a sign of inflammation that attributes to intimal hyperplesia (underlying pathology of AVF stenosis and thrombosis).

Opposite to our result, Li *et al.* (2022) a prospective cohort study collecting clinical basic data and laboratory parameters of a total 120 patients undergoing regular hemodialysis at the hemodialysis center of the First Affiliated Hospital of Jinan University from September 2017 to September 2018. It showed no significant correlation between albumin and AVF failure.

In relation to C Reactive protein (CRP), our study results show significant relationship between elevated CRP and AVF dysfunction.

This result is supported by the result of Stirbu *et al.* (2019) a Prospective observational cohort study conducted on 258 patients receiving an AVF between 2006 and 2016 at the Municipal Hospital Arad. Demographic, clinical, and laboratory characteristics were obtained at the time of AVF creation. The primary study end point was AVF patency loss which was defined as an event occurring at least 2 months after AVF formation and requiring surgical revision or replacement of the fistula. The patients were followed up for a median time of 26 months. It was found that CRP level was an independent predictor of AVF patency loss and CRP level may be a useful tool to predict AVF outcomes. It represents a strong predictor of AVF thrombosis events in HD patients. The high CRP level indicates presence of inflammation. Inflammation stimulates vascular smooth muscle cell proliferation in a platelet-derived growth factor-dependent manner and also enhances the endothelial synthesis of plasminogen activator inhibitor type 1, leading to neointima formation. Inflammatory mediators are associated with the proliferation of myofibroblasts and the migration of smooth muscle cells and the facilitation of a process like atherosclerosis. That could explain the correlation between CRP level and AVF outcome.

As CRP, we find positive relationship between Erythrocyte Sedimentation Rate (ESR) and the risk of having AVF failure in our study.

That is ok with Zadeh *et al.* (2021) an observational prospective cohort study enrolled 265 patients with ESRD on maintenance hemodialysis during a period of 3 years from 2016 to 2019. Their results had been evaluated after 4 months of fistula creation and its relation to laboratory tests as ESR and CRP levels and failure or maturation of AVFs were recorded in a checklist. It demonstrated a significant relation between raised ESR and loss of the patency of AVF. Elevated ESR indicates the presence of inflammation which is responsible of formation of neo-intimal hyperplesia.

Our results are against the result of Choi *et al.* (2015) a retrospective single center study including One-hundred fourteen HD patients receiving AVF operation. It reported no differences in CRP and ESR levels between the group with AVF failure and those with a functional AVF.

5. Conclusion

AVF is the vascular access of choice in hemodialysis patients as recommended by KIDGO. It has high rate of early and late failure. There are many risk factors affecting AVF maturity and patency leading to AVF failure, but Dyslipidemia, anemia, high platelets, high renal function, hypoalbuminemia, elevated ESR 1 hour, and CRP are the most independent risk factors for AVF failure regarding the multi-logistic regression analysis of this study.

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