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ORIGINAL ARTICLE

Impact of Diabetes Mellitus in Arteriovenous Fistula Dysfunction in Patients on Regular Hemodialysis

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Abstract

Background: **Primary arteriovenous fistula (AVF) failure has been linked to the existence of diabetes mellitus in some individuals, but not in all.**

Aim of the work: **The study's objective is to assess how diabetes mellitus affects individuals receiving regular hemodialysis (HD) who have AVF malfunction.**

Patient and methods: **All the 90 participants in this research had end-stage renal disease (ESRD) and were being treated with regular HD. The patients were divided into three groups according to their age and sex. Group A had 20 nondiabetic patients enrolled as the control group without any diagnosis of liver disease; Group B had 35 patients who were diabetic but were controlled where Hb A1C ≤ 7; Group C had 35 patients who are diabetic but are uncontrolled where Hb A1C > 7.**

Results: **This study showed the distribution of AVF failure in the three groups, where it failed in 4 (20%), 13 (37.1%), and 23 (65.7%) in groups A, B, and C, respectively. There was statistically substantial increase in AVF failure in groups B and C rather than group A, and in group C rather than group B.**

Conclusion: **People with diabetes as a whole had more primary AVF failure than patients without the disease. In addition compared with diabetic individuals with HbA1c values < 7%, those with HbA1c values ^{3}7% had a greater incidence of primary AVF failure.**

Keywords: Arteriovenous fistula, Chronic renal failure, Diabetes mellitus, HbA1c

1. Introduction

Diabetes type 2 is characterized by chronic hyperglycemia and abnormal carbohydrates, fat, and protein metabolism, which are due to either lack of insulin production or failure of its performance at the level of cells. The prevalence of diabetes has globally increased during the last two decades. The reported prevalence is 0.19% in people under 20 years of age and 8.6% in adults over the age of 20 years.[1]

Fasting hyperglycemia and impaired glucose tolerance are responsible for short- and long-term complications that affect all the body systems.[2]

Renal impairment is one of the major consequences of diabetics. The most popular kind of therapy with an arteriovenous fistula (AVF) is hemodialysis. Although hemodialysis was initially introduced by Kolf and colleagues in 1943, its routine application was delayed until 1960 because of the need for permanent access to vascular networks in prolonged hemodialysis.[3]

Vascular access failures, however, continue to be a serious issue in hemodialysis. The primary factor in hospital admissions and fatalities once the fistula is created is its related complications. Patients with ESRD pay more for therapy as a result of this.[4]

The ideal vascular access creates an appropriate flow for hemodialysis. Furthermore, it stays

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functional for a long period with minimal complications.[4]

The research aimed to assess the impact of diabetes mellitus in AVF dysfunction in patients on regular HD.

2. Patients and methods

This retrospective research was carried out at a dialysis center of the Department of Nephrology, Ahmed Maher Teaching Hospital, Cairo Governorate, Egypt.

This research was carried out on 90 patients (age and sex matched); all are ESRD on regular HD and will be divided into three groups.

Group A: 20 nondiabetic patients.

70 patients who are diabetic (more than 10 years) was subdivided into two groups. **Group B:** 35 patients who are diabetic (controlled). **Group C:** 35 patients who are diabetic (uncontrolled).

The research was carried out at the Bab El-Sharia, AL-Azhar University Hospital's Nephrology Department.

Inclusion criteria: Patients aged 30–60 years old, patients on regular HD sessions >6 months duration, and blood flow rate of 300–350 ml/minute.

Exclusion criteria: Maluses of needle<AQ: Pls check> (e.g.: hematoma), smoking, poor mobility, arm trauma, AV graft, and malignancy.

Operational design: The following information was gathered from each patient at the time of admission.

Initial assessment: Complete history, mentioning, personal data: Every patient had a customized page filled out with their name, age, sex, employment, residence, history of HTN or previous interventions, past medication use, family history of the illness, hospital diagnosis, date of admission in the hospital, and history of blood transfusions.

Clinical investigation focusing on: General: **vital signs** (temperature, pulse rate, blood pressure, and respiration rate), **signs of** jaundice, pallor, cyanosis, and swollen lymph nodes. **Chronic complications of diabetes mellitus**: skin infections, e.g., cellulitis and abscess, foot infection, e.g., diabetic foot, diabetic dermopathy, acanthosis nigricans.

Abdominal and local clinical examination: Abdominal inspection: Inspect the patient's **abdomen** for scars, swelling, pigmentation, and movement. **Abdominal palpation: Palpate** each of the **nine abdominal regions**, assessing for tenderness, rebound tenderness, guarding, or masses. **Abdominal percussion and abdominal auscultation**.

Investigations: comprehensive blood image: Red blood cells (RBCs), white blood cells (WBCs), platelet count, and hemoglobin level (Hb%). **Renal function test:** urine, blood urea, and serum creatinine analysis. **Liver function test:** HBA1C, prothrombin time (PT), international normalized ratio (INR), serum albumin, serum bilirubin, serum aspartate and alanine aminotransferases (AST and ALT), and Kt/v calculation using blood phosphorus, calcium, and intact parathyroid hormone.

Evaluation of AVF functions by Duplex Ultrasound: Pre-dialysis measures: venous blood flow rate, arterial blood flow rate, arterial diameter, and venous diameter.

Clinical evaluation: Measurement of arterial pressure during HD, measurement of venous pressure during HD, and evaluation of steal syndrome (ischemia of the hand brought on by a significant decrease in flow or reversal across the arterial segment distal to the AVF).

Procedure: The patient should be lying supine, with the arm that will be evaluated extended from the body at a 45-degree angle and turned externally. The patient should externally twist the leg to be checked whether the transplant was a leg loop.

Analyze the inflow artery in the transverse view before doing the fistula scan. For a comprehensive understanding of anatomy, scan the whole length of the access in this direction to the outflow vein. Rotate the view to longitudinal, then go back to the inflow artery. Pulsed Doppler examination should be performed on the native artery close to the access anastomosis to determine the peak systolic velocity (PSV) and end-diastolic velocity (EDV) (Fig. 1). Photograph the proximal anastomosis while capturing PSV and pulsed Doppler waveforms. Expect to detect spectrum widening and diastolic flow across this region rather than the triphasic waveforms often seen in peripheral arterial beds as the dialysis access offers low-resistance outflow to the arterial bed. Use color flow Doppler imaging as guidance for positioning the pulsed Doppler sample volume while you scan the rest of the access in longitudinal view.

2.1. Statistical analysis

The acquired information was tabulated and examined using SPSS version 25 (statistical tool for the social sciences) (Armonk, NY: IBM Corp). Using the Shapiro-Wilk and Kolmogorov-Smirnov tests, the data were examined for normality. Two different statistical methods were used: **Descriptive statistics**: Depending on the kind of data, mean ± SD was used to represent quantitative data, while numbers and percentages were used to express qualitative data. **Analytic statistics**: To compare three or more

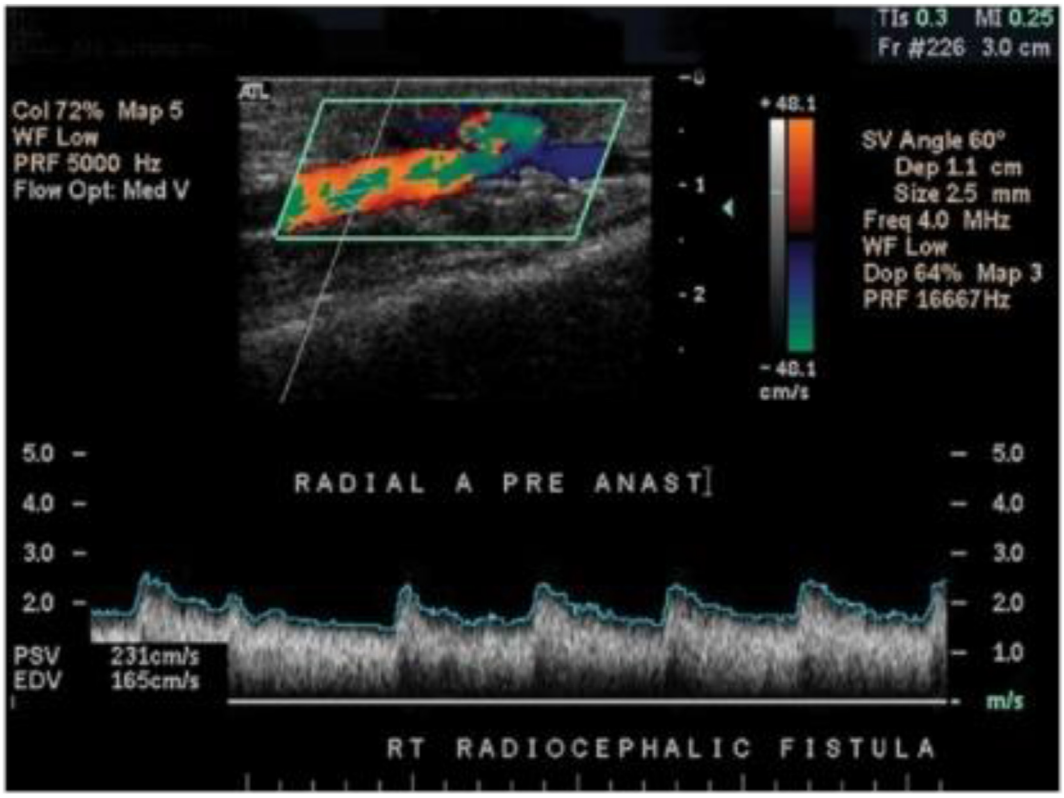

Fig. 1. The radial artery next to a Brescia-Cimino fistula exhibits spectrum widening, diastolic flow, and rise of both PSV and EDV, all of which are typical of arterial beds with low-resistance outflow. A normal radial artery will have triphasic waveforms with no spectrum widening and PSV >40 cm/s in the lack of dialysis access.

groups with parametric quantitative variables, the ANOVA (F) test is utilized. When comparing three or more groups using nonparametric quantitative variables, Kruskal–Wallis (H) test is used as a measure of significance. The comparison and relationship between two qualitative variables were studied using the Chi-square test ($\chi 2$). For two-tailed tests, a P-value of <0.05 or below was regarded as statistically significant, and <0.001 was regarded as very significant.

3. Results

A total of 90 cases were included in this research, age and sex matched, all were ESRD on regular HD, and the cases were split into three groups: **Group A:** Twenty (20) nondiabetic patients enrolled as the control group without any diagnosis of liver disease. **Group B:** Thirty-five (35) patients who are diabetic but are controlled where Hb A1C $\leq$ 7. **Group C:** Thirty-five (35) patients who are diabetic but are uncontrolled where Hb A1C > 7 Table 1.

This table shows that a comparison between the three groups showed that means of age and BMI were nearly equal between groups with no statistically substantial variation (P>0.05), where the median of age in group A was 50.80 ± 7.35, in group B was 51.91 ± 7.05, and in group C was 51.23 ± 5.23; and the BMI mean in group A was 30.98 ± 6.54, in group B was 28.26 ± 4.11, and in group C was 29.02 ± 5.70 Table 2.

This table shows the distribution of males and females in the three groups, where females were more prevalent 12 (60%), 20 (57.1%), and 18 (51.4%)

Table 1. Comparison of three groups in terms of age and BMI.

Variable	Groups			ANOVA test	
	Group A (number = 20) Mean ± SD	Group B (number = 35) Mean ± SD	Group C (number = 35) Mean ± SD	F	*P* value
Age (year)	50.80 ± 7.35	51.91 ± 7.05	51.23 ± 5.23	0.197	0.899
BMI	30.98 ± 6.54	28.26 ± 4.11	29.02 ± 5.70	1.66	0.196

*P value > 0.05 is insignificant.

Table 2. Comparison between three groups as regards Sex.

Sex	Groups				Chi-Square	
	Group A (number = 20) *N* (%)	Group B (number = 35) *N* (%)	Group C (number = 35) *N* (%)	Total *N* (%)	X^2	*P* value
Male	8 (40.0%)	15 (42.9%)	17 (48.6%)	40 (44.4%)		
Female	12 (60.0%)	20 (57.1%)	18 (51.4%)	50 (55.6%)	0.437	0.804
Total	20 (100.0%)	35 (100.0%)	35 (100.0%)	90 (100.0%)		

in groups A, B, and C, respectively. No statistically substantial variation was found by comparison between the three groups as regards Sex (P>0.05) Table 3.

This table shows the distribution of macroangiopathies as hypertension and coronary artery disease, and microangiopathies as retinopathy in the three groups, where there was a statistically substantial increase in hypertension, coronary artery disease, and retinopathy in patients in groups B and C rather than group A, which was found by comparison between three groups ($P < 0.05$) Table 4.

This table shows the distribution of AVF sites in the three groups, where brachiocephalic in 10 (50%), 18 (51.4%), and 20 (57.1%), and radiocephalic in 10 (50%), 17 (48.6%), and 15 (42.9%) in groups A, B, and C, respectively. No statistically substantial variation was found by comparison between the three groups as regards AVF site (P>0.05) Table 5.

This table shows the distribution of AVF failure in the three groups, where it failed in 4 (20%), 13 (37.1%), and 23 (65.7%) in groups A, B, and C, respectively. There was a statistically substantial increase in AVF failure in groups B and C rather

Table 3. Comparison between three groups regarding microangiopathies and macroangiopathies in diabetes.

	Groups				Chi-Square	
	Group A (number = 20) *N* (%)	Group B (number = 35) *N* (%)	Group C (number = 35) *N* (%)	Total *N* (%)	X^2	*P* value
Hypertension						
Yes	5 (25.0%)	20 (57.1%)	26 (74.3%)	51 (56.7%)	12.60	0.002*
No	15 (75.0%)	15 (42.9%)	9 (25.7%)	39 (43.3%)		
Coronary artery disease						
Yes	5 (25.0%)	19 (54.3%)	20 (57.1%)	44 (48.9%)	5.93	0.046*
No	15 (75.0%)	16 (45.7%)	15 (42.9%)	46 (51.1%)		
Retinopathy						
Yes	6 (30.0%)	22 (62.9%)	23 (65.7%)	51 (56.7%)		
No	14 (70.0%)	13 (37.1%)	12 (34.3%)	39 (43.3%)	7.50	0.023*
Total	20 (100.0%)	35 (100.0%)	35 (100.0%)	90 (100.0%)		

Table 4. Comparison between three groups as regards AVF site.

	Groups				Chi-Square	
	Group A (number = 20) *N* (%)	Group B (number = 35) *N* (%)	Group C (number = 35) *N* (%)	Total *N* (%)	X^2	*P* value
Brachiocephalic	10 (50.0%)	18 (51.4%)	20 (57.1%)	48 (53.3%)		
Radiocephalic	10 (50.0%)	17 (48.6%)	15 (42.9%)	42 (46.7%)	0.344	0.842
Total	20 (100.0%)	35 (100.0%)	35 (100.0%)	90 (100.0%)		

Table 5. Comparison between three groups as regards AVF failure.

	Groups				Chi-Square	
	Group A (number = 20) *N* (%)	Group B (number = 35) *N* (%)	Group C (number = 35) *N* (%)	Total *N* (%)	X^2	*P* value
Yes	4 (20.0%)	13 (37.1%)	23 (65.7%)	40 (44.4%)		
No	16 (80.0%)	22 (62.9%)	12 (34.3%)	50 (55.6%)	12.01	0.002*
Total	20 (100.0%)	35 (100.0%)	35 (100.0%)	90 (100.0%)		

than group A, which was found by comparison between the three groups ($P < 0.05$) Table 6.

This table shows the distribution of AVF dysfunction causes in the three groups, where there was thrombosis in 3 (15%) and stenosis 1 5%) in group A, and thrombosis in 7 (20%), steal syndrome in 2 (5.7%), stenosis in 3 (8.6%), and aneurism in 1 (2.9%) in group B, thrombosis in 9 (25.7%), steal syndrome in 5 (14.3%), stenosis in 8 (22.9%), and aneurism in 1 (2.9%) in group C. No statistically substantial variation was found by comparison between three groups as regards AVF dysfunction causes (P>0.05).

4. Discussion

When compared with arteriovenous grafts or central venous catheters, arteriovenous fistula (AVF) is often regarded as the finest access method for hemodialysis, offering the greatest long-term patency, lowest cost, and lowest infection rates.[5] A considerable portion of AVF, however, does not develop correctly to support dialysis treatment. Some writers[6] have shown that having diabetes mellitus increases the chance of developing vascular access failure. Other authors disagree with this finding.[7]

This current study shows that comparison between the three groups showed that means of age and BMI were nearly equal between groups with no statistically substantial variation (P>0.05), where the median of age in group A was 50.80 ± 7.35, in group B was 51.91 ± 7.05, and in group C was 51.23 ± 5.23 and the BMI mean in group A was 30.98 ± 6.54, in group B was 28.26 ± 4.11, and in group C was 29.02 ± 5.70.

This current study shows the distribution of males and females in the three groups, where females were more prevalent 12 (60%), 20 (57.1%), and 18 (51.4%), and in groups A, B, and C respectively. No statistically substantial variation was found by comparison between three groups as regards Sex (P>0.05).

HbA1C (glycemic control) with the results of AV FISTULAS: ROGAVF STUDY 2019: A total of 65 participants were enrolled in prospective observational research. The study population's median age was 54.7 years (SD: 12.6). Nearly 59% of them were men, with the remaining being women.[8]

However, in the study of **Jeong *et al.*,**[9] it was found that patients with type 2 diabetes were more likely to be obese ($P < 0.01$), where BMI was 24.2 ± 3.97 in the T2DM group vs 23.0 ± 3.31in the non-DM group.

This current research shows the distribution of hypertension, coronary artery disease, retinopathy in the three groups, where there was statistically substantial increase in hypertension, coronary artery disease, retinopathy in patients in groups B and C rather than group A, which was found by comparison between three groups ($P < 0.05$).

In accordance with our findings, the investigation of **Afsar & Elsurer,**[10] both with HbA1c ^{3}7% and with HbA1c ≤ 7%, nondiabetic individuals had a lower incidence of coronary artery illness, hypertension, and retinopathy than diabetic patients. Compared with diabetic individuals with HbA1c£7%, nondiabetic patients had a decreased incidence of cerebrovascular illness ($P = 0.03$ using Fisher's exact test).

Similarly, the study of **Afsar & Elsurer,**[10] when compared with nondiabetic individuals and diabetic patients with HbA1c £7%, diabetic patients with HbA1c^{3}7% had a lower C-reactive protein content among laboratory markers. Between nondiabetic individuals and diabetic patients with HbA1c ^{3}7%, hemoglobin levels varied, but not between other groups. Only between nondiabetic individuals and diabetic patients with HbA1c ^{3}7% the total cholesterol values were varied. All groups' serum glucose levels were significantly different from one another (P^{3}0.0001).

This current study shows the distribution of AVF site in the three groups, where brachiocephalic in 10 (50%), 18 (51.4%), and 20 (57.1%), and radiocephalic in 10 (50%), 17 (48.6%), and 15 (42.9%) in groups A, B, and C, respectively. No statistically significant difference was found by comparison between three groups as regards the AVF site (P>0.05).

Matching with our results were those of **Cruz *et al.*,**[11] where no statistically significant difference

Table 6. Comparison between three groups as regards AVF dysfunction causes.

	Groups				Chi-Square	
	Group A (number = 20) *N* (%)	Group B (number = 35) *N* (%)	Group C (number = 35) *N* (%)	Total *N* (%)	X^2	*P* value
Thrombosis	3 (15.0%)	7 (20.0%)	9 (25.7%)	19 (21.1%)		
Steal syndrome	0 (0.0%)	2 (5.7%)	5 (14.3%)	7 (7.8%)	14.32	0.074
Stenosis	1 (5.0%)	3 (8.6%)	8 (22.9%)	12 (13.3%)		
Aneurism	0 (0.0%)	1 (2.9%)	1 (2.9%)	2 (2.2%)		
None	16 (80.0%)	22 (62.9%)	12 (34.3%)	50 (55.6%)		
Total	20 (100.0%)	35 (100.0%)	35 (100.0%)	90 (100.0%)		

was found as regards AVF site, radiocephalic [28 (57.14%) VS 49 (49.49%) $P = 0.3894$], and brachiocephalic [10 (20.40%) VS 26 (26.26%) $P = 0.5425$] for diabetic and nondiabetic patients, respectively.

In the **Konner** *et al.*[12] study for both diabetic and nondiabetic individuals, different percentages of three different fistula types were developed: forearm AV fistula (24%, 62%), perforating vein fistula (PVF) at the elbow (48%, 21%), and non-PVF at the elbow (29%, 17%).

This current study shows the distribution of AVF failure in the three groups, where it failed in 4 (20%), 13 (37.1%), and 23 (65.7%) in groups A, B, and C, respectively. There was a statistically substantial increase in AVF failure in groups B and C rather than group A, which was found by comparison between three groups ($P < 0.05$).

Matching with our results, a review of studies linking diabetic individuals to AVF failure in hemodialysis was conducted by **Yan** *et al.*[13]

In consistent with our results, **Singh** *et al.*[8] who found that an HbA1c of less than 6.5 is related with a very high likelihood of AVF maturity at 6 weeks after formation (AOR = 22.65, $P < 0.005$), indicating that individuals with adequate diabetes management are more likely to have AVF maturity than those with HbA1c 6.5 or higher.

This current study shows the distribution of AVF dysfunction causes in the three groups, where thrombosis in three (15%) and stenosis 1 (5%) in group A, and thrombosis in 7 (20%), steal syndrome in 2 (5.7%), stenosis in 3 (8.6%), and aneurism in 1 (2.9%) in group B, thrombosis in 9 (25.7%), steal syndrome in (14.3%), stenosis in 8 (22.9%), and aneurism in 1 (2.9%) in group C. No statistically substantial variation was found by comparison between three groups as regards AVF dysfunction causes (P>0.05).

Similarly, to our results **Konner** *et al.*[12] found that in patients with diabetes and those without diabetes, thromboses were responsible for three and seven occurrences per 100 patient-years at risk, respectively. This overall variation was statistically substantial ($P = 0.01$). Only one of the 181 diabetic individuals and 18 of the 567 nondiabetic participants had an early thrombosis during the first month after the installation of the access. Steal syndrome-related peripheral ischemia is a well-known side effect of AV shunting. Peripheral ischemia was statistically significantly different in diabetes and nondiabetic patients, accounting for 7 and 0.6 occurrences per 100 patient years at risk, on average, across all access types ($P < 0.0001$).

Diabetes raises the likelihood of platelet aggregation and raises von Willebrand factor secretion, which encourages platelet aggregation and damages blood vessel endothelial cells.[14]

In conclusion, we discovered that in diabetic people, poor glycemic control as measured by HbA1c may be a significant risk factor for the emergence of primary AVF failure. It is probable that variations in glycemic control among diabetic individuals account in part for disparities in AVF failure between diabetic and nondiabetic people. We think further research is required to support our results and demonstrate the pathophysiologic connection between primary AVF failure and higher HbA1c levels and determining if measures to lower HbA1c levels would increase AVF patency. To assess the long-term fate of fistulae in people with diabetes, further research is necessary.

4.1. Conclusion

People with diabetes as a whole had more primary AVF failure than patients without the disease. In addition, compared with diabetic individuals with HbA1c values < 7%, those with HbA1c values ≥ 7% had a greater incidence of primary AVF failure.

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

All authors have a substantial contribution to the article.

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Conflicts of interest

The authors declared that there were no conflicts of interest.

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