

Diabetes Mellitus Affecting Arteriovenous Fistula (AVF)

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ABSTRACT

Introduction: Diabetes is one of the main contributors to chronic kidney disease (CKD) and end-stage renal disease (ESRD), conditions that often require hemodialysis. An arteriovenous fistula (AVF), a connection surgically created between an artery and a vein, is the preferred vascular access method for dialysis due to its longevity and lower risk of infection. AVF outcomes in diabetic patients are often compromised due to diabetes-related vascular issues, including endothelial injury arterial calcification and reduced blood flow. **Aim of the study:** The study aimed to evaluate the risk factors contributing to AVF, focusing on the history of diabetes in these patients. **Methods & Materials:** This observational study was conducted at Dhaka Medical College Hospital (DMCH) to assess AVF outcomes in CKD stage 5 and ESRD patients needing AVF construction. Eighty-two participants, meeting specific inclusion and exclusion criteria, were enrolled from January 2019 to July 2020. Clinical history, physical examination, and peripheral pulse assessments were performed. Blood samples were taken for various lab investigations. Following AVF construction, patients were closely monitored every 7-10 days and evaluated in weeks six and ten for AVF status. **Result:** In a study involving 82 patients, the arteriovenous fistula (AVF) failure rate was found to be 28%, while 72% of AVFs functioned successfully. Patients in the failure group were slightly older (mean age 47.13 years) and had a higher body mass index (BMI) (24.66 kg/m²). The failure group exhibited significantly lower systolic (SBP) and diastolic blood pressure (DBP) compared to the functioning

group. Notably, diabetes mellitus (DM) was present in 73.9% of the failure group, with smoking and BMI also correlating significantly with AVF failure. Increased BMI and smoking were associated with higher odds of AVF failure, emphasizing the need for careful patient management. **Conclusion:** This study reveals that diabetes significantly increases the early failure rate of arteriovenous fistulas (AVFs) in CKD and ESRD patients, with a 28% failure rate. Key risk factors include high BMI, smoking, and low diastolic blood pressure (DBP), while age and serum creatinine levels showed no significant differences.

Keywords: Diabetes, Arteriovenous fistula (AVF), chronic kidney disease (CKD) and End-stage renal disease (ESRD)

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INTRODUCTION

The number of patients with chronic kidney disease (CKD) and end-stage renal disease (ESRD) is increasing worldwide. The global prevalence of CKD is estimated to be around 843.6 million individuals worldwide in 2017 [1]. The prevalence of ESRD patients is increasing by around 7-9% every year. Vascular access is mandatory for maintenance hemodialysis [2]. Arteriovenous fistula (AVF) is the preferred vascular access for hemodialysis (HD). The arteriovenous fistula (AVF) is an anastomosis created between a native artery and vein [3]. It is the preferred dialysis access for most patients with end-stage renal disease (ESRD) due to long-term benefits, including less morbidity and mortality, fewer rates of infection and

complications, and lower costs compared to other types of vascular accesses. However, these benefits are limited by the risk of AVF failure and maturation failure in up to 60% of these patients [4]. Studies have a different definition of primary failure. However, early failure is defined as AVF never maturing to support dialysis or failure within three months of use and is diagnosed as thrombosis and immediate failure of the fistula [5,6]. The risk of early failure was 23% but increased to 37% in older people [6]. Dysfunctional AVF is a significant cause of morbidity, overall mortality, and excess costs. For this reason, several vital predictors of AVF failure were identified [7]. Diabetes is a leading cause of kidney failure and has an increasing prevalence globally [8]. Within the UK, about

20,000 people with diabetes die prematurely, and renal disease accounts for 11% and 21% of deaths in people with type 1 and type 2 diabetes, respectively [9]. Diabetic patients with end-stage renal failure requiring renal replacement therapy in the form of hemodialysis are best managed with an autologous AVF [10]. Establishing a functioning AVF can be challenging because fistula maturation remains a complex and multifactorial process, with the vascular remodeling of both arteries and veins being affected by many factors [11]. Diabetic patients are predisposed to a higher incidence of peripheral vascular disease than people without diabetes, with poorer flow rates and a burden of arterial wall calcification [12]. As a result, patients undergoing radio-cephalic AVFs have historically experienced poorer outcomes than non-diabetic counterparts, leading to the misconception that diabetic patients should be excluded from AVF eligibility and directed toward alternative vascular access options. Using ultrasound to appraise the suitability of vessels pre-fistula formation, Vessel mapping has significantly improved outcomes for fistulas in all patients, including those with diabetes. It is now recommended by the National Kidney Foundation Kidney Dialysis Outcome Quality Initiative [13]. Despite this recommendation, there remains variation in results, which is reflected in variations in practice [13,14]. Due to the high incidence of primary AVF failure, which can significantly impact the long-term morbidity and mortality of patients with ESRD on hemodialysis, this study was conducted to evaluate the risk factors contributing to AVF, with a particular focus on the history of diabetes in these patients.

METHODOLOGY & MATERIALS

This was an observational study. All patients with CKD 5 and ESRD were assessed accordingly and attended indoors and outdoors in the Department of Nephrology, Dhaka Medical College Hospital (DMCH), Dhaka, Bangladesh. After selecting participants according to the inclusion and exclusion criteria, they were approached for inclusion in the study. A total of eighty-two patients with CKD stage 5 and ESRD who require AVF construction were included in this study from January 2019 to July 2020. History-taking focused on clinical features, and a physical examination was done. All peripheral pulses were scrutinized. Ethical approval was taken from DMC's Ethical Review Committee (ERC). Following the information about the study's aim, objectives, and procedure, informed written consent was obtained from each participant.

Inclusion criteria:

- Age more than 18 years.
- CKD Stage 5 and ESRD patients who require AVF construction.

Exclusion criteria:

- Active infection.
- Diagnosed case of CLD.
- History of previous AVF failure.
- Pregnancy.

Investigations including CBC, S. hs CRP, S. Albumin, S. Ferritin, and Fibrinogen were done. For these investigations, 8-10 ml of blood was collected through venipuncture from the antecubital site using an aseptic method. For the serum hs CRP, ferritin, and albumin test, 3 ml of blood was taken within the sample clotted activator tube, then 10 minutes kept in the rack, centrifuged with 3500 rotation per minute (RMP) for 15 minutes. After getting all the required reports, they were referred to the Department of Urology and Vascular Surgery of DMCH for AVF construction. After the AVF construction study, patients were followed up with a clinical examination of AVF (inspection, palpation, and auscultation) every 7 to 10 days.

If any complication (sign of infection, bleeding, hematoma, sign of AVF failure) or any features prone to AVF failure were observed for further management, they were consulted with respective surgeons (department) and acted accordingly. Particularly in the sixth and tenth week of AVF construction, participants were followed up. During follow-up, participants were examined thoroughly, and special attention was paid to AVF, including inspection, palpation (thrill), auscultation (bruit), pulse augmentation test, and arm elevation test for clinical evaluation of AVF status. AVF status was either failure or functioning. Then, data was enrolled in either AVF failure or AVF functioning groups. Finally, participant's age, sex, smoking history, BMI, DM, S. hs CRP, S. Ferritin, S. Fibrinogen, S. Albumin, and NLR with early AVF failure were analyzed.

Data collection

A questionnaire was prepared considering key variables like demographic data, clinical presentation, clinical findings, and investigations, which were collected, verified by the guide, and collected by the researcher. After the selection of the patient, the aims, objectives, and procedures of the study were explained in understandable language to the patient. Risks and benefits were also made clear to the patient. The patients were encouraged to participate and allowed to withdraw from the study. Then, informed written consent was taken from each patient.

Statistical analysis

Statistical analysis was done using the Statistical Package for Social Sciences version 25.0 for Windows (SPSS Incl., Chicago, Illinois, USA). Continuous variables were expressed as mean±SD and categorical variables as frequencies and proportions. The relationship between independent and dependent variables was analyzed using the Chi-square test, logistic regression test, and unpaired t-test. Statistical significance was assumed when the probability value was less than 0.05.

RESULT

A total of 82 patients participated in this study. AVF status exhibited a failure rate of 28%, whereas a promising 72% of AVFs were found to be functioning correctly (Figure 1). The mean age of patients in the AVF failure group was 47.13 years, slightly higher than the 45.31 years in the AVF functioning group. BMI was higher in the AVF failure group (24.66 kg/m²)

compared to the AVF functioning group (22.07 kg/m²). The AVF failure group exhibited statistically lower SBP (134.13 mm Hg) and DBP (63.7 mm Hg) compared to the AVF functioning group, where these values were higher (147.51 mm Hg for SBP and 80.81 mm Hg for DBP) (Table 1). MAP followed a similar trend, being lower in the AVF failure group (87.17 mm Hg) compared to the AVF functioning group (102.51 mm Hg). Serum Creatinine levels were comparable between the two groups, with 7.91 mg/dL in the AVF failure group and 7.94 mg/dL in the AVF functioning group. The AVF failure group had significantly higher BMI and lower SBP, DBP, and MAP than the AVF functioning group. At the same time, age and serum creatinine levels showed no significant differences between the two groups (Table I). Almost half of the patients were female in the AVF failure group and 25(42.4%) in the AVF functioning group (Figure 2). Most patients had distal AVF, with 82.6% in the AVF failure group and 83.1% in the AVF functioning group (Figure 3). Significant differences were observed in BMI categories, where a higher percentage of patients with BMI <18.5 kg/m² were found in the AVF functioning group (25.4%) compared to the AVF failure group (8.7%). Relative to the AVF functional group (44.1%), the presence of DM was considerably more significant in the AVF failure group (73.9%). In the AVF failure group, there was a more significant proportion of smokers (56.5%) than in the AVF functional group (32.2%) (Table 2). The mean age of DM patients (50.19 years) was significantly higher than non-DM patients (41 years). Gender distribution showed a higher percentage of males in the DM group (65.1%) compared to the non-DM group (46.2%), although this difference did not reach statistical significance. DBP was

significantly lower in DM patients than in non-DM participants. The inflammation markers, including serum high-sensitivity C-reactive protein (hs CRP), serum albumin, and serum ferritin, did not significantly differ between DM and Non-DM groups. Individuals with DM had much higher fibrinogen levels (394.15 mg/dl) than those of non-diabetic individuals (308.43 mg/dl) (Table 3). Table 4 analyzes the association of risk factors related to AVF failure. Odds ratios indicated that a higher BMI was associated with increased odds of AVF failure (OR = 1.014, p = 0.019). Similarly, smoking history showed a significant association (OR = 1.039, p = 0.014). In contrast, other factors such as age, gender, and the presence of DM did not exhibit significant associations with AVF failure (p > 0.05).

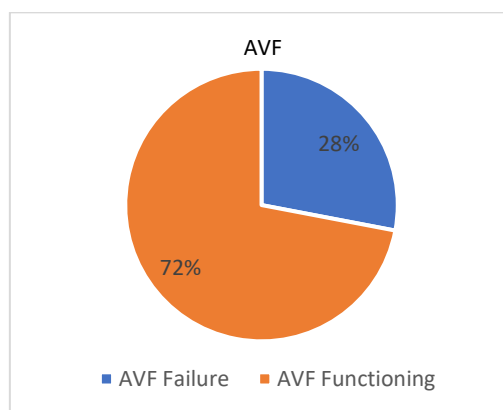


Figure – 1: AVF status.

Table – I: Distribution of the study patients by baseline characteristics (n=82)

Baseline characteristics	AVF Failure (n=23)	AVF Functioning (n=59)	p-value
	Mean ± SD	Mean ± SD	
Age (years)	47.13±13.48	45.31±10.78	0.525
BMI (kg/m ²)	24.66±3.17	22.07±3.43	0.002
SBP (mm hg)	134.13±21.3	147.51±15.77	0.002
DBP (mm hg)	63.7±12.72	80.81±14.61	0.001
MAP (mm hg)	87.17±11.6	102.51±13.26	0.001
S. Creatinine (mg/dl)	7.91±1.7	7.94±1.43	0.935

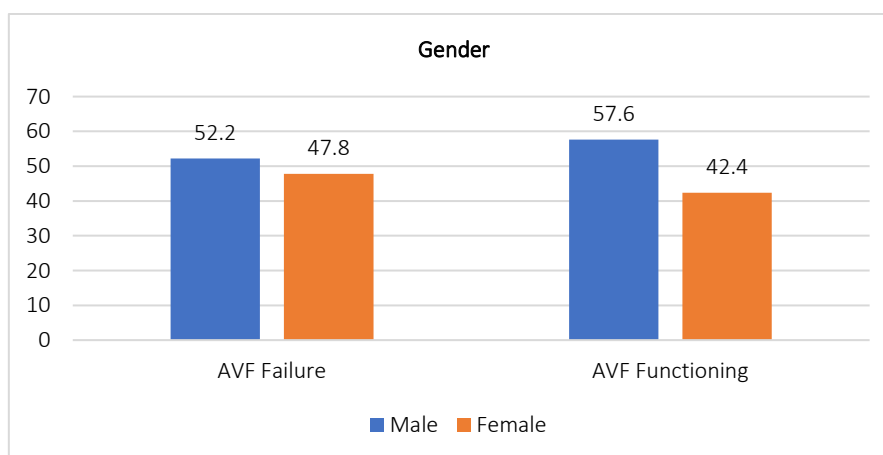


Figure – 2: Gender distribution of the study population based on AVF status

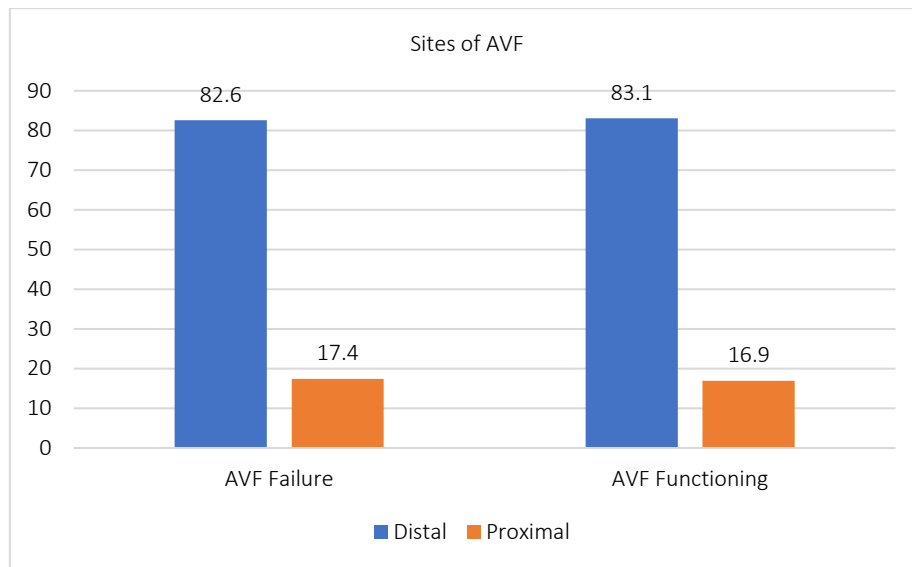


Figure - 3: Site of AVF based on AVF status

Table - II: Distribution of the study patients by clinical and risk factors profile (n=82)

Clinical variables	AVF Failure (n=23)		AVF Functioning (n=59)		p-value
	n	%	n	%	
BMI (kg/m²)					
<18.5	2	8.7	15	25.4	0.008s
18.5-22.9	4	17.4	25	42.4	
23.0-27.5	10	43.5	11	18.6	
>27.5	7	30.4	8	13.6	
Presence of DM					
Yes	17	73.9	26	44.1	0.015s
No	6	26.1	33	55.9	
Smoking history					
Yes	13	56.5	19	32.2	0.043s
No	10	43.5	40	67.8	

Table - III: Baseline characteristics analysis of the patients between DM and Non-DM (n=82)

Baseline characteristics	DM (n=43)		Non-DM (n=39)		p-value
	n	%	n	%	
Age (years) Mean ± SD	50.19±11.3		41±9.88		0.001
Gender					
Male	28	65.1	18	46.2	0.084
Female	15	34.9	21	53.8	
Smoking history	17	39.5	15	38.5	0.92
	Mean±SD		Mean±SD		
BMI (kg/m ²)	23.24±3.18		22.3±3.88		0.234
DBP (mm hg)	71.28±15.4		81.23±15.22		0.004
S. hs CRP (mg/l)	21.79±24.8		11.58±10.95		0.02
S. Albumin (g/l)	31±6.61		33.56±5.78		0.066
S. Ferritin (micg/l)	495.78±410.89		439.99±357.99		0.472
Fibrinogen (mg/dl)	394.15±178.54		308.43±129.34		0.015

Table – IV: Association of risk factors relate to AVF failure (n=82)

Characteristics	OR	95% CI		p-value
		Lower	Upper	
Age	0.78	0.633	0.96	0.681ns
Gender	0.264	0.037	1.88	0.184ns
DM	0.378	0.073	1.959	0.246ns
BMI	1.014	0.948	1.085	0.019s
Smoking	1.039	0.998	1.082	0.014s
SBP	0.08	0.011	0.601	0.063ns
DBP	1.06	1.004	1.12	0.036s

DISCUSSION

Chronic kidney disease is a public health problem, and its prevalence is increasing [15]. Among hemodialysis patients, arteriovenous fistula use is also increasing [16,17]. Functioning AVF is mandatory for maintenance hemodialysis [2]. This observational study was carried out to identify, explore, and estimate the factors associated with AVF failure, focusing on the history of diabetes in these patients. According to our study, 28% (23 participants) of AVFs have been identified to be failing, and 72% (59 participants) of AVFs were found to be operating normally. Bahrami-Ahmadi et al. found 30 cases of early AVF failure and 370 cases of non-early AVF failure [18]. This study found that the participants' mean age was 47.13±13.48 years in the AVF failure group and 45.31±10.78 years in the AVF functioning group. The association between age and early AVF failure was insignificant (P=0.525). Khavanin Zadeh M et al. found that the mean age was 53.27±17.47 years [2]. This study showed that high BMI was significantly associated with early AVF failure. Mean BMI was 24.66±3.17 (kg/m²) and 22.07±3.43 (kg/m²) in the AVF failure and functioning groups, respectively. Kaygin, MA et al. found that BMI was 22.6±4.2 (kg/m²) and 21.9±4.6 (kg/m²) in the AVF failure and functioning groups, respectively [19]. Segal et al. also found that high BMI was associated with early AVF failure, similar to this study [20]. These studies also found that comparatively low DBP and low MAP were associated with early AVF failure. In 2019, Pandey et al. found that diastolic and mean arterial blood pressures were significantly associated with early AVF failure, similar to this study [21]. Low BP was a risk for early AVF failure due to the formation of thrombosis in AVF [22]. Serum Creatinine levels showed no significant difference in this present study. There was no significant difference between males and females with AVF failure. Similarly, Kaygin, MA et al. found no significant difference between males and females with early AVF failure [19]. Pandey et al. found that the early AVF failure rate of females (33.3%) was higher than that of males (24.6%) and was insignificant, which was not similar to this study [21]. Female gender was associated with a high rate of early AVF failure, which may be due to veins in women being less likely to dilate and low caliber vessels [17]. The data indicates that most patients in both the AVF failure and AVF functioning groups had distal AVF. This high prevalence of distal AVF in both groups suggests that the location of the AVF (distal vs. proximal) is not a distinguishing factor for AVF outcomes in this study population. Creating an AVF in the non-dominant distal forearm (radiocephalic site) is preferred, with early

failure rates ranging from 5% to 41%. Alternatively, the upper arm or a proximal site can be chosen for AVF placement, where early failure rates range from 2% to 26% [23]. A significant association between DM and early AVF failure was found in this study. Similarly, Hernandez T et al. illustrated that DM was a strong risk factor for early AVF failure [24]. Obesity and DM were associated with increased inflammatory markers such as CRP, which can precipitate the initial development of AVF thrombosis and stenosis leading to early AVF failure [25,26]. Conversely, Tang et al. reported the results of a prospective observational study that arteriovenous fistula maturation did not have a significant difference in diabetic and non-diabetic renal failure patients [27]. Gordon et al. reported the same result, where the maturation and prognosis of arteriovenous fistula did not differ significantly between diabetic and non-diabetic patients. Diabetes is not one of the exclusion factors for the use of arteriovenous fistula access because diabetic patients have the same maturation results as non-diabetic patients [28]. Smoking was significantly associated with early AVF failure, which was similar to another study. Ozdemir et al. found the association between smoking and early AVF failure in their study [29]. Significant differences were observed in the two groups, including age, diastolic blood pressure (DBP), serum high-sensitivity C-reactive protein (hs CRP) levels, and fibrinogen levels. Age was notably higher in the DM group compared to the non-DM group. DBP was lower in the DM group, while his CRP and fibrinogen levels were higher in the DM group than in non-DM. Other parameters such as gender distribution, smoking history, body mass index (BMI), serum albumin, and serum ferritin levels did not show statistically significant differences between the groups. These findings suggest that age, DBP, hs CRP, and fibrinogen levels may significantly distinguish baseline characteristics between diabetic and non-diabetic patients, potentially influencing outcomes in clinical settings. The results of our study are comparable with the findings of Santosa et al. and Afsar et al. [30,31]. This study found that age and sex did not influence the development of early AVF failure. However, smoking, high BMI, DM, comparative low blood pressure (DBP MAP), and high serum hs CRP were associated with early arteriovenous fistula failure. In multivariate logistic regression analysis of age, sex, BMI, DM, smoking, SBP, and DBP status, the effect on failure of AVF was evaluated; BMI, smoking, and comparative low DBP were significantly associated with AVF failure.

Limitations of the study:

This study has several limitations that should be acknowledged. The study was conducted in a single center, which may introduce selection bias and limit the diversity of the patient population. Furthermore, the reliance on clinical assessments for AVF status may not capture all complications, potentially leading to underreporting of AVF failure. Confounding factors such as medications, comorbid conditions, and lifestyle variations were not controlled for, which could affect the outcomes.

CONCLUSION

In conclusion, this study highlights that diabetes significantly contributes to the early failure of arteriovenous fistulas (AVFs) in patients with chronic kidney disease (CKD) and end-stage renal disease (ESRD). The failure rate of AVFs was 28%, with a notable association between high body mass index (BMI), smoking, and low diastolic blood pressure (DBP) with AVF failure. Although age and serum creatinine levels showed no significant differences between groups, the presence of diabetes (73.9% in the failure group) correlated strongly with adverse AVF outcomes. These findings underscore the importance of addressing modifiable risk factors in managing AVF success in diabetic patients.

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Conflict of interest: None declared.

Ethical approval: The study was approved by the Institutional Ethics Committee.

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