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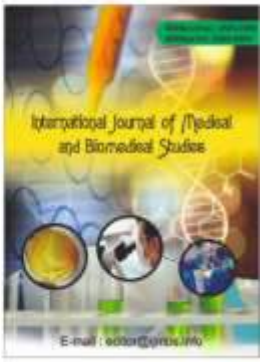

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Original Research Article

Age, Sex, and Hemoglobin Levels Influence Arteriovenous Fistula Failure in Chronic Kidney Disease Patients

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Abstract:

Persons with chronic kidney disease (CKD) are increasing in number every year. End-stage CKD patients experience damage to kidney structure and function, therefore need kidney replacement therapy such as hemodialysis. Hemodialysis (HD) requires access to the bloodstream i.e. arteriovenous fistula (AVF) which is a permanent and most widely used HD access route. Arteriovenous fistulas are influenced by various factors that can affect their success for HD. The purpose of this study was to determine the relationship of age, sex, and Hb levels with AVF failure in CKD patients. This study used a cross-sectional design in 89 patients in whom an AVF was created. The study was conducted from February to June 2023, using secondary data from patient medical records according to inclusion criteria from January to December 2022 at a private hospital in Pekanbaru, Sumatra, Indonesia. Data analysis was carried out using the chi-squared test at a significance level of $p<0.05$. The majority of respondents in this study were aged 46-59 years and 62 (69.7%) were females. Mean Hb level was 9.15±0.92 g/dL and patients with diabetes and hypertension accounted for 51.7% and 73%, respectively. The results of the chi-squared test of age, sex, and Hb levels with AVF failure showed a significant relationship at $p=0.045$, $p=0.029$, and $p=0.005$, respectively. This study showed that there was a significant association of age, sex, and Hb levels with AVF failure in CKD patients.

Keywords: age, sex, Hb level, AVF failure, chronic kidney disease

Introduction

Chronic kidney disease (CKD) is a condition where the kidneys are damaged such that there is an irreversible and progressive loss of function. Based on data from the Basic Health Research (*Riskesdas*) for 2018, the number of patients increased by 1.8% as compared with 2013, namely from 2% to 3.8%. The increase in the number of CKD patients started from the age of 35 – 44 years (3.31%) and continued to rise up to the age of 65 – 74 years (8.23%). In Indonesia 12.5% of the total population has CKD.[1,2]

When CKD has reached the final stage or end state renal disease, the kidneys do not function normally and the patient needs renal replacement therapy, such as hemodialysis. Hemodialysis (HD) needs an access route to the bloodstream and the

frequently used route is the arteriovenous fistula (AVF), created by connecting the patient's artery with a vein. An AVF is recommended because it can be used in the long term, although there are cases where an AVF cannot be used or fails after being used a number of times.[3,4]

There are several factors that can influence the outcomes of an AVF, namely age, sex, and the presence of comorbidities, such as diabetes mellitus and hypertension. In addition to above-mentioned factors, the hemoglobin concentration (Hb) may reportedly also influence the AVF results. The study of Gjorgjievski et al. reported that age is an absolute risk factor and male sex is associated with better AVF maturation, at a p-value of 0.018, such that the probability of failure is lower, but the study by Satrio et al. stated that both age and sex do not affect AVF failure. Regarding the Hb concentration, there are still few studies on the relationship between AVF failure and Hb concentration, such that the present investigators wished to study the relationship of age, sex, and Hb concentration with AVF failure in patients with CKD.[5–7]

Methods

This was an observational analytical study of cross-sectional design. The study was conducted from February to June 2023 using secondary data from the electronic medical records of patients undergoing surgery for the creation of an AVF in the Awal Bros Hospital, Pekanbaru, West Sumatra, Indonesia, from January to December 2022 with a sample size of 89 patients that were recruited by consecutive non-random sampling. The inclusion criteria in this study were firstly patients with CKD who underwent HD, were aged 35-70 years, and had a history of AVF access creation of at least 4 weeks, and secondly the existence of pre-operative Hb concentration examination results for AVF creation. An AVF creation is said to be successful if there is maturation in 4-6 weeks that meets the following requirements on ultrasound examination, i.e. 1. being located approximately 0.6 Cm from the skin surface, 2. having blood velocities of > 600 mL/minute, 3. having a blood vessel diameter of > 0.6 Cm. If the patient does not fulfill the above-mentioned requirements then the AVF access creation is said to have failed.[8] Pre-operative Hb concentration prior to AVF creation is categorized into <9.9 g/dL and ≥ 9.9 g/dL.[6] Data analysis was by means of the chi-squared test, with a p-value of <0.05 being considered significantly different. This study obtained ethical clearance from the Research Ethics Committee, Faculty of Medicine, Universitas Trisakti, under no. 18/KER-FK/I/2023.

Results

Table 1: Distribution of study characteristics

Characteristics	n (%)	$\bar{x}$±SD
Age (years)		54.41±9.90
35 – 45	12 (13.5)	
46 – 59	43 (48.3)	
≥ 60	34 (38.2)	
Sex		
Male	27 (30.3)	
Female	62 (69.7)	
Hb concentration (g/dL)		9.15±0.92
< 9.9	52(58.43)	
≥ 9.9	37(41.57)	
Diabetes Mellitus		
Yes	46 (51.7)	
No	43 (48.3)	
Hypertension		
Yes	65 (73.0)	
No	24 (27.0)	

Table 1 shows the data on the characteristics of the study subjects. It was found that the majority of patients had an age range of 46 – 59 years (48.3%), were female (69.7%), and had a history of diabetes mellitus (51.3%) and hypertension (75%).

Table 2: Relationship of age, sex, and Hb concentration with AVF failure

Variable	AVF failure				p
	Yes (n)	%	No (n)	%	
Age (years)					
35 – 45	7	58.4	5	41.6	0.045*
46 – 59	17	39.5	26	60.5	
≥ 60	23	67.7	11	32.3	
Sex					
Male	19	70	8	30	0.029*
Female	28	45	34	55	
Hb concentration (g/dL)					
< 9.9	34	65.4	18	34.6	0.005*
≥ 9.9	13	35.1	24	64.9	

* Chi-squared test, $p < 0.05$ = significantly different

The study results in Table 2 show that in 23 patients (67.7%) aged ≥ 60 years there was a significant relationship between age and AVF failure, at p value = 0.045. Furthermore, in the case of sex and AVF failure, a significant relationship was found, at a p-value of 0.029. For Hb concentration and AVF failure, the results showed that AVF failure was more frequently found in patients with Hb concentration < 9.9 g/dL (65.4%), at p value = 0.005.

Discussion

The results of this study show that most of the subjects were 46 – 59 years old. This is in line with the study of Satria et al. stating that the age range of the majority of patients with chronic kidney disease (CKD) who underwent surgery for AVF was 45 - 60 years.[9] This is because the renal mass starts to decrease between 30 and 80 years of age. In the normal aging process of the kidneys, 30% of the glomeruli become damaged, while in the remaining 70% of the glomeruli there are disorders of filtration capacity. According to the Centers for Disease Control and Prevention (CDC**),** CKD frequently occurs at the age above 40 years, when the filtration capacity of the kidneys decreases by around 1% annually.[10] In addition, other conditions that can cause kidney damage are hypertension and diabetes mellitus (DM) with the highest prevalence at the ages of 55 – 64 years.[11] In this study we found that the majority of subjects who underwent AVF creation, namely 46 persons (51.3%), had a history of DM. These results are in agreement with those of the study by Sari et al. who found a significant relationship between DM and CKD.(11) One of the renal complications of DM may be the appearance of diabetic nephropathy. The majority of the subjects (65 subjects or 73%) who underwent AVF creation had hypertension. This is in line with the study of Sari et al, in that the majority of patients (57 subjects or 73.1%) who underwent AVF creation had hypertension.(7) One study reported that hypertension was one of the principal causes of end state renal disease, because hypertension causes damage in the glomeruli by influencing the arteries that cause a reduction in the blood flow to the kidneys.[12] Patients with end state renal disease need a treatment to replace the kidneys, namely HD that uses AVF access.[12,13]

Based on Table 2, the study results on sex show that most of the subjects are female, at 62 subjects (69.7%). These results agree with the study of Sari et al., where the subjects were mostly female at 50.5%[11], but not with the study by Wilmink et al., who found more created AVFs in males at 473 (59%) than in females at 330 (41%).[14] The National Kidney

Foundation states that the cause of the sex difference is still undetermined, but that females more frequently have urinary tract infections capable of causing kidney damage and therefore are at higher risk of kidney damage from pregnancy problems such as hypertension or eclampsia.[15]

The results of this study showed that the mean Hb concentration of the patients was 9.15 ± 0.92 g/dL. This may have been caused by the fact that anemia in patients with CKD is a frequently seen complication. The mechanism of the occurrence of anemia may be because many factors such as a progressively decreasing erythropoietin concentration, iron deficiency that may be caused by anemia, abnormal absorption of iron, ineffective use of iron reserves, systemic inflammation, decreased bone marrow response, reduced red cell life span, and deficiencies of vitamin B12 or folic acid.[16,17]

The results of this study showed that there was a significant relationship between age and AVF failure (p=0.045). These study results are in line with the study conducted by Hod et al. showing that age ≥ 67 years was associated with AVF failure.[18] The study by Sari et al. stated that easily found arterial stiffness as well as comorbidities in elderly persons that may cause decreased vascular elasticity, ultimately leading to failure of AVF creation.[7]

The results of the analysis for sex and AVF failure showed that failure tends to occur in males (70%), as compared to that in females (43 %). These results show a significant relationship between sex and AVF failure (p=0.029). These results are in line with the study of Salmela et al., where sex is associated with a decrease in the potential use of the fistula, and also in line with the study by Gjorgjievski et al., stating that sex was associated with AVF maturation.[5,19] The exact mechanism of the sex difference is still not known with certainty, but reportedly the cause may lie in the difference in vascular diameter, reactivity, and abnormal venous dilation in the presence of arterial pressure. [20]

Our study results show that failure tends to occur in patients with a pre-operative Hb concentration of < 9.9 g/dL (65.4%), signifying that there is a significant relationship between Hb concentration and AVF failure (p=0.005). These results are in line with another study that was conducted by Zadeh et al.[21], stating that low Hb concentrations were a higher factor of AVF failure in patients with Hb <8 g/dL with relative risk 1.41 and p=0.01.[21] Similar results were found in the study by Satrio et al. who stated that Hb concentrations of <9.9 g/dL had a high risk of AVF creation failure,[6] the mechanism of which is still unclear and under study. However, reportedly low Hb concentrations may induce low grade inflammation in the body, causing hyperplasia of the intima and resulting in a high probability of thrombosis at the anastomosis site, resulting in AVF failure. Therefore it is said that patients with CKD who have anemia are at greater risk of AVF failure.[17,22,23]

The present study has implications for the management of patients with CKD who require AVF creation for HD, in that before doing AVF creation, the clinician should pay attention to the age, sex, and Hb concentration of the patients to reduce the risk of AVF creation failure. The conclusion of this study is that there is a significant relationship of age, sex, and Hb concentration with AVF failure. Further studies are necessary in patients with CKD to obtain more information or data on the hematocrit, the use of erythropoietin stimulating agents, and the duration of comorbidities such as hypertension or diabetes.

Acknowledgment

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Original Research Article

Age, Sex, and Hemoglobin Levels Influence Arteriovenous Fistula Failure in Chronic Kidney Disease Patients

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Corresponding author: Pusparini

Conflict of interest: No conflict of interest

Abstract:

Persons with chronic kidney disease (CKD) are increasing in number every year. End-stage CKD patients experience damage to kidney structure and function, therefore need kidney replacement therapy such as hemodialysis. Hemodialysis (HD) requires access to the bloodstream i.e. arteriovenous fistula (AVF) which is a permanent and most widely used HD access route. Arteriovenous fistulas are influenced by various factors that can affect their success for HD. The purpose of this study was to determine the relationship of age, sex, and Hb levels with AVF failure in CKD patients. This study used a cross-sectional design in 89 patients in whom an AVF was created. The study was conducted from February to June 2023, using secondary data from patient medical records according to inclusion criteria from January to December 2022 at a private hospital in Pekanbaru, Sumatra, Indonesia. Data analysis was carried out using the chi-squared test at a significance level of $p<0.05$. The majority of respondents in this study were aged 46-59 years and 62 (69.7%) were females. Mean Hb level was 9.15±0.92 g/dL and patients with diabetes and hypertension accounted for 51.7% and 73%, respectively. The results of the chi-squared test of age, sex, and Hb levels with AVF failure showed a significant relationship at $p=0.045$, $p=0.029$, and $p=0.005$, respectively. This study showed that there was a significant association of age, sex, and Hb levels with AVF failure in CKD patients.

Keywords: age, sex, Hb level, AVF failure, chronic kidney disease

Introduction

Chronic kidney disease (CKD) is a condition where the kidneys are damaged such that there is an irreversible and progressive loss of function. Based on data from the Basic Health Research (*Riskesdas*) for 2018, the number of patients increased by 1.8% as compared with 2013, namely from 2% to 3.8%. The increase in the number of CKD patients started from the age of 35 – 44 years (3.31%) and continued to rise up to the age of 65 – 74 years (8.23%). In Indonesia 12.5% of the total population has CKD.[1,2]

When CKD has reached the final stage or end state renal disease, the kidneys do not function normally and the patient needs renal replacement therapy, such as hemodialysis. Hemodialysis (HD) needs an access route to the bloodstream and the

frequently used route is the arteriovenous fistula (AVF), created by connecting the patient's artery with a vein. An AVF is recommended because it can be used in the long term, although there are cases where an AVF cannot be used or fails after being used a number of times.[3,4]

There are several factors that can influence the outcomes of AVF, namely age, sex, and the presence of comorbidities, such as diabetes mellitus and hypertension. In addition to above-mentioned factors, the hemoglobin concentration (Hb) may reportedly also influence the AVF results. The study of Gjorgjievski et al. reported that age is an absolute risk factor and male sex is associated with better AVF maturation, at a p-value of 0.018, such that the probability of failure is lower, but the study by Satrio et al. stated that both age and sex do not affect AVF failure. Regarding the Hb concentration, there are still few studies on the relationship between AVF failure and Hb concentration, such that the present investigators wished to study the relationship of age, sex, and Hb concentration with AVF failure in patients with CKD.[5–7]

Methods

This was an observational analytical study of cross-sectional design. The study was conducted from February to June 2023 using secondary data from the electronic medical records of patients undergoing surgery for the creation of an AVF in the Awal Bros Hospital, Pekanbaru, West Sumatra, Indonesia, from January to December 2022 with a sample size of 89 patients that were recruited by consecutive non-random sampling. The inclusion criteria in this study were firstly patients with CKD who underwent HD, were aged 35-70 years, and had a history of AVF access creation of at least 4 weeks, and secondly the existence of pre-operative Hb concentration examination results for AVF creation. An AVF creation is said to be successful if there is maturation in 4-6 weeks that meets the following requirements on ultrasound examination, i.e. 1. being located approximately 0.6 Cm from the skin surface, 2. having blood velocities of > 600 mL/minute, 3. having a blood vessel diameter of > 0.6 Cm. If the patient does not fulfill the above-mentioned requirements then the AVF access creation is said to have failed.[8] Pre-operative Hb concentration prior to AVF creation is categorized into <9.9 g/dL and ≥ 9.9 g/dL.[6] Data analysis was by means of the chi-squared test, with a p-value of <0.05 being considered significantly different. This study obtained ethical clearance from the Research Ethics Committee, Faculty of Medicine, Universitas Trisakti, under no. 18/KER-FK/I/2023.

Results

Table 1: Distribution of study characteristics

Characteristics	n (%)	$\bar{x}$±SD
Age (years)		54.41±9.90
35 – 45	12 (13.5)	
46 – 59	43 (48.3)	
60	34 (38.2)	
Sex		
Male	27 (30.3)	
Female	62 (69.7)	
Hb concentration (g/dL)		9.15±0.92
< 9.9	52(58.43)	
≥ 9.9	37(41.57)	
Diabetes Mellitus		
Yes	46 (51.7)	
No	43 (48.3)	
Hypertension		
Yes	65 (73.0)	
No	24 (27.0)	

Table 1 shows the data on the characteristics of the study subjects. It was found that the majority of patients had an age range of 46 – 59 years (48.3%), were female (69.7%), and had a history of diabetes mellitus (51.3%) and hypertension (75%).

Table 2: Relationship of age, sex, and Hb concentration with AVF failure

Variable	AVF failure				p
	Yes (n)	%	No (n)	%	
Age (years)					
35 – 45	7	58.4	5	41.6	0.045*
46 – 59	17	39.5	26	60.5	
≥ 60	23	67.7	11	32.3	
Sex					
Male	19	70	8	30	0.029*
Female	28	45	34	55	
Hb concentration (g/dL)					
< 9.9	34	65.4	18	34.6	0.005*
9	13	35.1	24	64.9	

* Chi-squared test, p < 0.05 = significantly different

The study results in Table 2 show that in 23 patients (67.7%) aged ≥ 60 years there was a significant relationship between age and AVF failure, at p value = 0.045. Furthermore, in the case of sex and AVF failure, a significant relationship was found, at a p-value of 0.029. For Hb concentration and AVF failure, the results showed that AVF failure was more frequently found in patients with Hb concentration < 9.9 g/dL (65.4%), at p value = 0.005.

Discussion

The results of this study show that most of the subjects were 46 – 59 years old. This is in line with the study of Satria et al. stating that the age range of the majority of patients with chronic kidney disease (CKD) who underwent surgery for AVF was 45 - 60 years.[9] This is because the renal mass starts to decrease between 30 and 80 years of age. In the normal aging process of the kidneys, 30% of the glomeruli become damaged, while in the remaining 70% of the glomeruli there are disorders of filtration capacity. According to the Centers for Disease Control and Prevention (CDC), CKD frequently occurs at the age above 40 years, when the filtration capacity of the kidneys decreases by around 1% annually.[10] In addition, other conditions that can cause kidney damage are hypertension and diabetes mellitus (DM) with the highest prevalence at the ages of 55 – 64 years.[11] In this study we found that the majority of subjects who underwent AVF creation, namely 46 persons (51.3%) had a history of DM. These results are in agreement with those of the study by Sari et al. who found a significant relationship between DM and CKD.[11] One of the renal complications of DM may be the appearance of diabetic nephropathy. The majority of the subjects (65 subjects or 73%) who underwent AVF creation had hypertension. This is in line with the study of Sari et al, in that the majority of patients (57 subjects or 73.1%) who underwent AVF creation had hypertension.[7] One study reported that hypertension was one of the principal causes of end state renal disease, because hypertension causes damage in the glomeruli by influencing the arteries that cause a reduction in the blood flow to the kidneys.[12] Patients with end state renal disease need a treatment to replace the kidneys, namely HD that uses AVF access.[12,13]

Based on Table 2, the study results on sex show that most of the subjects are female, at 62 subjects (69.7%). These results agree with the study of Sari et al., where the subjects were mostly female at 50.5%[11], but not with the study by Wilmink et al., who found more created AVFs in males at 473 (59%) than in females at 330 (41%).[14] The National Kidney

Foundation states that the cause of the sex difference is still undetermined, but that females more frequently have urinary tract infections capable of causing kidney damage and therefore are at higher risk of kidney damage from pregnancy problems such as hypertension or eclampsia.[15]

The results of this study showed that the mean Hb concentration of the patients was 9.15 ± 0.92 g/dL. This may have been caused by the fact that anemia in patients with CKD is a frequently seen complication. The mechanism of the occurrence of anemia may be because many factors such as a progressively decreasing erythropoietin concentration, iron deficiency that may be caused by anemia, abnormal absorption of iron, ineffective use of iron reserves, systemic inflammation, decreased bone marrow response, reduced red cell life span, and deficiencies of vitamin B12 or folic acid.[16,17]

The results of this study showed that there was a significant relationship between age and AVF failure (p=0.045). These study results are in line with the study conducted by Hod et al. showing that age ≥ 67 years was associated with AVF failure.[18] The study by Sari et al. stated that easily found arterial stiffness as well as comorbidities in elderly persons that may cause decreased vascular elasticity, ultimately leading to failure of AVF creation.[7]

The results of the analysis for sex and AVF failure showed that failure tends to occur in males (70%), as compared to that in females (43 %). These results show a significant relationship between sex and AVF failure (p=0.029). These results are in line with the study of Salmela et al., where sex is associated with a decrease in the potential use of the fistula, and also in line with the study by Gjorgjievski et al., stating that sex was associated with AVF maturation.[5,19] The exact mechanism of the sex difference is still not known with certainty, but reportedly the cause may lie in the difference in vascular diameter, reactivity, and abnormal venous dilation in the presence of arterial pressure. [20]

Our study results show that failure tends to occur in patients with a pre-operative Hb concentration of < 9.9 g/dL (65.4%), signifying that there is a significant relationship between Hb concentration and AVF failure (p=0.005). These results are in line with another study that was conducted by Zadeh et al.[21], stating that low Hb concentrations were a higher factor of AVF failure in patients with Hb <8 g/dL with relative risk 1.41 and p=0.01.[21] Similar results were found in the study by Satrio et al. who stated that Hb concentrations of <9.9 g/dL had a high risk of AVF creation failure.[6] the mechanism of which is still unclear and under study. However, reportedly low Hb concentrations may induce low grade inflammation in the body, causing hyperplasia of the intima and resulting in a high probability of thrombosis at the anastomosis site, resulting in AVF failure. Therefore it is said that patients with CKD who have anemia are at greater risk of AVF failure.[17,22,23]

The present study has implications for the management of patients with CKD who require AVF creation for HD, in that before doing AVF creation, the clinician should pay attention to the age, sex, and Hb concentration of the patients to reduce the risk of AVF creation failure. The conclusion of this study is that there is a significant relationship of age, sex, and Hb concentration with AVF failure. Further studies are necessary in patients with CKD to obtain more information or data on the hematocrit, the use of erythropoietin stimulating agents, and the duration of comorbidities such as hypertension or diabetes.

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