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Risk Factors of Catheter-Related Infection in Patients Undergoing Hemodialysis Using Double Lumen Catheter at Dr. M. Djamil Hospital Padang

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ABSTRACT

Background. Chronic kidney disease (CKD) is a terminal disease requiring hemodialysis. Hemodialysis requires vascular access using a double lumen catheter (DLC). However, the use of DLC may increase complications mainly infection, either infection of exit site or bloodstream. This study is aimed to seek risk factors contributing to the incidence of central catheter-related infections in CKD patients with DLC undergoing HD at Dr. M. Djamil Hospital, Padang. **Methods.** This study is a prospective study on patients undergoing HD at Dr. M. Djamil Hospital, Padang. This study using consecutive sampling technique. Data were analyzed using SPSS version 25.0. **Results.** This study involved 40 CKD patients undergoing HD. Majority of the samples had bloodstream infections (67.5%). Clinical manifestations of purulent secretion, duration of catheter used, and hypoalbuminemia had significant differences in the incidence of DLC infection based on bloodstream infection and exit site infection ($p<0.05$). The most common bacterial found was *Pseudomonas aeruginosa* (22.5%) which was sensitive to ceftazidime, cefepime, meropenem, amikacin, gentamicin, ciprofloxacin. **Conclusion.** Factors contributing to the incidence of DLC-related infections at Dr. M. Djamil Hospital are duration of catheter use and hypoalbuminemia. *Pseudomonas aeruginosa* is the most common cause of DLC-related infections.

1. Introduction

Chronic kidney disease (CKD) is a significant public health problem. The number of events increases yearly, and when it reaches a terminal stage hemodialysis is required as a substitute for kidney function to survive.[1] Globally, the estimated number of individuals affected by CKD is as many as 843.6 million.[2] Recent data show the global incidence and prevalence of CKD during 1990-2016 increased by 89 and 87%, respectively, and reached 100% in countries with medium and low sociodemographic indices. It is estimated that there has been a twofold increase in the number of deaths from CKD in the last three decades, shifting CKD from the 18th leading cause of death in 1990 to the 11th in 2016.[2]

Hemodialysis (HD) is the most common renal replacement therapy modality in patients with CKD, with a prevalence of up to 89%.[3,4] In Indonesia, the Report of the Indonesian Renal Registry reports that the number of new patients and active patients in Indonesia undergoing HD 2018 has doubled fold.[5] In 2017 there were 30,831 new patient cases and 77,892 active patients, while in 2018, there were 66,433 new patient cases and 132,142 active patients.[6]

Adequate hemodialysis depends on access to large blood vessels capable of providing rapid and stable blood flow.[7] Autogenous arteriovenous fistulas (AVF) is the first choice for permanent vascular access but require a minimum of six weeks to be used.[8] One method to achieve hemodialysis access quickly is central venous catheterization using a double lumen catheter (DLC). DLC is widely used for acute purposes and a bridge to more permanent vascular access such as mature AVF.[9] The use of a temporary DLC has several advantages, including practicality, rapid insertion, direct use, and painlessness during dialysis.[10] However, the use of temporary DLC increases the risk of developing complications such as thrombosis and infection. Infections due to DLC use can cause catheter dysfunction and increase mortality by more than 50%, and cause significant morbidity in the dialysis population.

Infections in the bloodstream, exit-site, and tunnel in the use of DLC reduce the effectiveness of therapy, cause complications of bacteremia and sepsis that increase the risk of death in patients with kidney failure and increase the use of health costs.[11] This study describes the risk factors for infection associated with catheter use using a double lumen catheter at Dr. M. Djamil Hospital, Padang.

2. Methods

This study design was an analytical study with a prospective approach. The participants were all patients undergoing hemodialysis at Dr. M. Djamil Hospital Padang from October to November 2021. A consecutive sampling process carried out the collection of research subjects. This research has been approved by the Health Research Ethics Committee of Dr. M. Djamil Hospital Padang (No.453/KEPK/2021).

This study observed the location of catheter insertion, duration of use, the presence of diabetes mellitus comorbidity, hypoalbuminemia, and infection due to the use of a double lumen catheter. Double lumen catheter infection was measured by blood culture taken from a peripheral vein and culture of the tip of a central venous catheter and purulent secretions at the insertion site. Participants were declared hypoalbuminemia if the serum albumin level was less than 3.5 g/dL. The presence of diabetes mellitus comorbidity and duration of catheter use were observed from medical records.

Data analysis was carried out using SPSS version 25 software. Univariate analysis was used to see the distribution of data for each variable and then presented in tabular form. The data consists of the baseline characteristics of the research sample. Categorical data are presented in terms of frequency, while continuous data are presented in mean and standard deviation.

Before the bivariate analysis was carried out, the normality of the data was tested using the Kolmogorov Smirnov test or the Shapiro Wilk test. An Independent T-test was performed to assess the relationship between factors related to the incidence of infection associated with a double lumen catheter in patients undergoing hemodialysis. Data were analyzed at 95% confidence intervals; if a p-value <0.05 was obtained, it could be concluded that there was a statistically significant relationship and difference in each hypothesis.

3. Results

A total of 40 patients became participants in this study. Table 1 showed the baseline characteristics of the participants in this study.

Table 1. Baseline characteristics participants

Characteristics	Double lumen catheter infection		p-value
	Bloodstream infection	Exit-site infection	
Age, mean±SD	53,89±9,53	53,54±9,58	0,914ᵃ
Gender, frequency (%)			1,000ᵇ
Male	17 (65,4)	9 (34,6)	
Female	10 (71,4)	4 (28,6)	
CKD etiology, frequency (%)			
Diabetes mellitus	14 (63,6)	8 (36,4)	0,812ᵇ
Hypertension	12 (70,6)	5 (29,4)	0,986ᵇ
Other cause	1 (100,0)	0	n/aᵇ
Clinical manifestation of infection, frequency (%)			
Hyperemia	8 (66,7)	4 (33,3)	1,000ᵇ
Purulent secretion	6 (31,6)	13 (68,4)	<0,001ᵇ*
Fever or shivering	27 (100,0)	0	n/aᵇ
Albumin level, mean±SD	3,05±0,41	3,13±0,50	0,599ᵃ

*p<0,05 significant; a: Independent sample T test; b: Chi-square test; n/a: not available.

There are no differences in age, gender, etiology of CKD, clinical manifestations in the form of hyperemia and fever/ shivering, and albumin levels on the incidence of DLC infection based on the type of infection, namely bloodstream infections and exit-site infections (p>0.05) in table 1. However, there was a significant difference in clinical manifestations of purulent secretions on the incidence of DLC infection based on bloodstream infection and exit-site infection (p<0.05). While in table 2, it can be seen that the majority of subjects experienced bloodstream infections, as many as 67.5%.

Table 2. The proportion of double lumen catheter (DLC)-associated infections in hemodialysis patients.

DLC infection	**frequency (%)**
Bloodstream infection	27 (67,5)
Exit-site infection	13 (32,5)

The relationship between insertion site, duration of use, comorbid DM, and hypoalbuminemia with the incidence of DLC-related infections in patients undergoing HD at RSUP Dr. M. Djamil Padang can be seen in table 3 as follows.

Table 3. Relationship of the insertion site, duration of use, comorbid DM and hypoalbuminemia with the incidence of DLC-related infections

Variable	DLC infection		p-value	HR (95% CI)
	Bloodstream infection (frequency, %)	Exit-site infection (frequency, %)		
Insertion location			0,859[b]	
Jugular vein	22 (68,8)	10 (31,3)		2,20 (0,13-38,83)
Subclavial vein	4 (66,7)	2 (33,3)		2,00 (0,08-51,59)
Femoral vein	1 (50,0)	1 (50,0)		0,46 (0,03-8,02)
Lengths of use			0,045[b*]	
≤ 14 days	1 (50,0)	1 (50,0)		Ref
> 14 days	26 (68,4)	12 (31,6)		1,92 (1,11-33,30)
Diabetes mellitus			1,000[b]	
Yes	14 (63,6)	8 (36,4)		0,67(0,18-2,59)
No	13 (72,2)	5 (27,8)		Ref
Hypoalbuminemia	20 (64,5)	11 (35,5)	0,036[b*]	1,91 (1,19-4,37)

Notes. b: Chi-square test; *p<0,05 Significant; Ref, reference.

In table 3, it is known that bloodstream infections are the most common type of infection at all insertion sites, namely 68.8% in the jugular vein, 66.7% in the subclavian vein, and 50% in the femoral vein. Of all subjects, 80% had an infection at the jugular vein insertion. Based on the results of statistical tests, it was found that there was no relationship between the insertion site and the incidence of DLC-related infections in patients undergoing HD (p>0.05).

The majority of the subjects experienced DLC infection with the duration of catheter use > 14 days. In subjects with DLC use more than 14 days, bloodstream infection was the most common type of infection (68.4%). Based on the results of statistical tests, it is known that there is a relationship between duration of use and the incidence of infection in patients using DLC >14 days (p<0.05). The probability of an increased risk of bloodstream infection with DLC >14 days was 1.92 (95% CI 1.11-33.30).

In patients with diabetes mellitus, bloodstream infections were more common (63.6%) than exit-site infections (36.4%). Based on the results of statistical tests, it is known that there is no relationship between comorbid diabetes mellitus and the incidence of DLC-related infections in patients undergoing HD ($p>0.05$).

Patients with hypoalbuminemia had more bloodstream infections (64.5%) than exit-site infections (35.5%). Based on the results of statistical tests, it was found that there was a relationship between hypoalbuminemia and the incidence of DLC-related infections in patients undergoing HD ($p<0.05$). The chance of risk of bloodstream infection in patients with low albumin levels was 1.91 (95% CI 1.19-4.37).

Table 4. Microbes patterns in cases of DLC-associated infections in patients undergoing HD

Microbes pattern	**Frequency (%)**
Staphylococcus aureus	7 (17,5)
Staphylococcus epidermidis	5 (12,5)
Staphylococcus aureus (MRSA)	4 (10,0)
Pseudomonas aeruginosa	9 (22,5)
Acinetobacter baumanni	1 (2,5)
Enterobacter cloacae complex	5 (12,5)
Enterococcus faecalis	4 (10,0)
Escherichia coli	3 (7,5)
Pantoea sp.	1 (2,5)
Klebsiella pneumoniae	1 (2,5)

Table 4 shows that the most common bacterial pattern in cases of DLC infection in patients undergoing HD is Pseudomonas aeruginosa (22.5%). In comparison, the pattern of germs and antimicrobial sensitivity in cases of DLC-related infections in patients undergoing HD at Dr. M. Djamil Hospital Padang can be seen in table 5 as follows.

Table 5. Bacterial patterns and antimicrobial sensitivity in cases of DLC-associated infections.

Microbes pattern	**Antimicrobial sensitivity**	**Frequency (%)**
Staphylococcus aureus	gentamicin, ciprofloxacin, levofloxacin, moxifloxacin, erythromycin, clindamycin, vancomycin, tetracycline, trimethoprim/ sulfamethoxazole	7 (17,5)
Staphylococcus epidermidis	gentamicin, ciprofloxacin, levofloxacin, moxifloxacin, erythromycin, clindamycin, vancomycin, tetracycline, trimethoprim/ sulfamethoxazole	3 (7,5)
	gentamicin, ciprofloxacin, levofloxacin, moxifloxacin, vancomycin, tetracycline	1 (2,5)
	clindamycin, vancomycin, tetracycline	1 (2,5)
Staphylococcus aureus (MRSA)	gentamicin, ciprofloxacin, levofloxacin, moxifloxacin, erythromycin, clindamycin, vancomycin, tetracycline, trimethoprim/ sulfamethoxazole	3 (7,5)
	gentamicin, ciprofloxacin, levofloxacin, moxifloxacin, erythromycin, clindamycin, vancomycin, trimethoprim/ sulfamethoxazole	1 (2,5)
Pseudomonas aeruginosa	ceftazidime, cefepime, meropenem, amikacin, gentamicin, ciprofloxacin	9 (22,5)
Acinetobacter baumanni	None	1 (2,5)
Enterobacter cloacae complex	meropenem, amikacin, gentamicin	4 (10,0)
	cefepime, meropenem, amikacin	1 (2,5)
Enterococcus faecalis	ceftazidime, cefepime, meropenem, amikacin, gentamicin, ciprofloxacin	2 (5,0)
	benzylpenicillin, ampicillin, gentamicin high level, streptomycin high level, levofloxacin, vancomycin, tetracycline	1 (2,5)
	benzylpenicillin, ampicillin, gentamicin high level, streptomycin high level, ciprofloxacin, levofloxacin, vancomycin, tetracycline	1 (2,5)
Escherichia coli	ampicillin / sulbactam, cefazoline, ceftazidime, ceftriaxone, cefepime, meropenem, amikacin, gentamicin, ciprofloxacin, trimethoprim / sulfamethoxazole	1 (2,5
	meropenem, gentamicin, trimethoprim / sulfamethoxazole	1 (2,5)
	meropenem, amikacin	1 (2,5)
Pantoea sp.	ampicillin / sulbactam, ciprofloxacin	1 (2,5)
Klebsiella pneumoniae	meropenem, amikacin	1 (2,5)

Table 5 shows that the most common bacteria found in cases of DLC-related infections in patients undergoing HD are *Pseudomonas aeruginosa* and sensitive to antimicrobials ceftazidime, cefepime, meropenem, amikacin, gentamicin, ciprofloxacin, which is 22.5%.

4. Discussion

In this study, there were 40 patients undergoing hemodialysis at Dr. M. Djamil Hospital Padang with the average age of patients with DLC infection, both bloodstream infection and exit-site infection were 53.89±9.53 years and 53.54±9.58 years, respectively. These results follow previous research by Gupta et al. (2016), who conducted a study to determine the clinical profile of hemodialysis patients who experienced DLC-related infections. The results showed that the average age of the patients was 53±14 years.[12] Based on the theory, elderly patients have decreased immune function and an increased risk of various CKD-related comorbidities such as hypertension and diabetes mellitus. In addition, patients with older age have a higher risk of developing complications from CKD.

In this study, diabetes mellitus was the most common etiology of CKD, rather than hypertension. However, there was no difference in CKD etiology in this study on the incidence of DLC infection based on bloodstream infection and exit-site infection (p> 0.05). Grothe et al. (2010) found that diabetes mellitus increased the risk of bloodstream infection by 1.37 times in CKD patients taking DLC.[14] Theoretically, elderly patients with diabetes mellitus comorbidity are risk factors that can increase the incidence of infection. Elderly patients with diabetes have decreased organ function. Organ dysfunction will cause immune system disorders, which will increase the risk of infection.

Clinical manifestations of patients with DLC infection may include hyperemia, purulent secretions, and fever or chills. There was a significant difference in the manifestation of purulent secretions in bloodstream infections (31.6%) and exit-site infections (68.4%) (p<0.05). Exit-site infection was defined as the finding of purulent secretions at the exit site or two of the three symptoms, namely erythema, tenderness and induration around the exit site.[14]

The mean albumin level in this study was found to be 3.05±0.41 in bloodstream infections and 3.13±0.50 in exit-site infections. Albumin levels had no difference against DLC infection based on bloodstream infection and exit-site infection (p>0.05). Jaudah et al. (2017) reported a mean albumin level of 3.2 ± 0.5 g/dL in patients with DLC-associated infections, but there was no association between albumin levels and the incidence of DLC-associated infections.[15]

We also found that DLC-related infections mostly occurred in bloodstream infections (67.5%) than exit site infections (32.5%). Menegueti et al. (2017) reported the incidence of DLC-related infections in patients undergoing hemodialysis. There were 22% cases of DLC infection, with 69% of cases of bacteremia and 31% of local infections. The incidence of DLC-associated infections that become bloodstream infections is 6.1 per 1000 days, and exit site infections are 2.7 per 1000 days.[16] DLC-associated bloodstream infections are associated with bacteria invasion originating from the skin flora around the catheter insertion or health workers during the catheter insertion, use, or maintenance. Bacteria enter from the skin to the bloodstream. Bacteria originating from both the external and the lumen of the catheter will form a biofilm. The state of this bacterial biofilm will cause a decrease in the effect of systemic antibiotics which will worsen the incidence of infection in the patient's bloodstream.

From the results was also obtained that 80% of patients experienced infection at the jugular vein insertion. Based on the results of statistical tests, it was found that there was no relationship between the insertion site and the incidence of DLC-related infections in patients undergoing HD (p>0.05). Basri et al. reported that more cases of DLC-related infection occurred at the insertion site of the femoral vein (23.5%) compared to the jugular or subclavian vein. Theoretically, the femoral vein is an infectious factor due to the accumulation of sweat and moisture in the application area.[17]

The majority of the subjects experienced DLC infection with the duration of catheter use more than 14 days. In subjects with DLC use more than 14 days, bloodstream infection was the most common type of infection (68.4%). In this study, only two subjects experienced DLC infection with catheter use < 14 days, with the same proportion in each type of infection. Based on the results of statistical tests, it is known that there is a relationship between duration of use and the incidence of DLC-related infections in patients undergoing HD ($p<0.05$). The risk of bloodstream infection with catheter use >14 days is 1.92 (95% CI 1.11-33.30). Shoaib et al. reported that the incidence of DLC-associated infections was more common in patients with a mean use of catheter duration of 27.4 ± 6.05 days.[18] Theoretically, the duration of catheter use depends on the location of the DLC insertion. Patients with a femoral vein insertion site can have five days of insertion, while patients with a jugular and subclavian vein insertion can have 21 days of insertion. However, based on the KDOQI (2019) guidelines, the use of DLC > 14 days is not recommended. Gupta et al. reported a significant association between the incidence of DLC-associated infections and the duration of DLC insertion ($p<0.001$). The use of DLC > 14 days will increase the incidence of DLC-related infections.

In patients with diabetes mellitus, bloodstream infections were more common (63.6%) than exit-site infections (36.4%). Based on the results of statistical tests, it is known that there is no relationship between diabetes mellitus comorbidity and the incidence of DLC-related infections in patients undergoing HD ($p>0.05$). Basri et al. reported no significant relationship between the incidence of diabetes mellitus comorbidity and DLC-related infections.[17] Patients with diabetes mellitus have a decrease in the immune system, leading to an increased risk of infection. In general, diabetes mellitus is an independent risk factor for infection. However, in some cases, diabetes alone is not a risk factor for infection unless accompanied by other conditions.

Patients with hypoalbuminemia had more bloodstream infections (64.5%) than exit-site infections (35.5%). Based on the results of statistical tests, it was found that there was a relationship between hypoalbuminemia and the incidence of DLC-related infections in patients undergoing HD ($p<0.05$). The probability of risk of bloodstream infection in hypoalbuminemia patients was 1.91 (95% CI 1.19-4.37). Ghonemy et al. reported that low albumin levels were significantly associated with the incidence of DLC-associated infections.[19] Knezevic et al. also reported that patients with hypoalbuminemia had a significant association with the incidence of DLC-associated bloodstream infections ($p=0.041$). Hypoalbuminemia in hemodialysis patients occurs due to malnutrition and contributes to bacterial infections.[20]

The most common bacterial patterns in cases of DLC infection in patients undergoing hemodialysis were *Pseudomonas aeruginosa* (22.5%), followed by *Staphylococcus aureus* (17.5), *Staphylococcus epidermidis* (12.5%), *Enterobacter cloacae* complex (12.5%), *Staphylococcus aureus* (MRSA) (10.0%), *Enterococcus faecalis* (10.0%), *Escherichia coli* (7.5%), *Acinetobacter baumanni* (2.5%), *Patoea sp.* (2.5%) and *Klebsiella pneumoniae* (2.5%). Gupta et al. reported that the most common microorganisms found in DLC-associated infections were *Staphylococcus aureus* (45.2%) isolated from catheter swabs, followed by *Pseudomonas aeruginosa* (17%), *Acinetobacter sp.* (9%), *Enterobacter spp.* (7.5). %) and *Klebsiella pneumoniae* (5.6%).[12] Meanwhile, the most common bacteremia culture was caused by *P. aeruginosa* in 38.8% of cases. Hussain et al. reported that the etiology of DLC-related infections was *Staphylococcus* (28.68%) followed by *Staphylococcus aureus* (21.32%).[21] Microorganisms that are commonly found, such as *Staphylococcus epidermidis* and *Staphylococcus aureus*.

5. Conclusion

There are differences in the clinical manifestations of purulent secretions on the incidence of DLC infection based on bloodstream infections and exit-site infections. Furthermore, there is a relationship between duration of use and hypoalbuminemia with the incidence of DLC-related infections. The most common germs found in DLC-related infections in hemodialysis patients were *Pseudomonas aeruginosa*.

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