



Factor Related to the Incidence of Ascites in Chronic Kidney Disease Patients Undergoing Hemodialysis at North Lombok Hospital

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ABSTRACT:

Introduction. Chronic kidney disease (CKD) is characterized by abnormalities in kidney function and structure, as well as kidney damage that lasts more than three months. Chronic kidney disease is still a problem in nephrology, with a relatively high incidence rate and a fairly broad and complex etiology. Nephrogenic ascites is a rare condition that can occur in patients with end-stage renal disease (ESRD) who have had long-term hemodialysis (HD). Ascites is one of the clinical parameters of fluid overload conditions in HD patients. The objective of this study was to identify the risk factors for ascites in CKD patients.

Method. This study was a cross-sectional study that was conducted at the North Lombok Hospital from September to November 2023. The study participants were end-stage CKD patients who had undergone hemodialysis. The total sampling technique was used for sampling. The information came from medical records. On each research variable, the Chi square test was used for analysis. A statistically significant p value was less than 0.05.

Results. This study enlisted the participation of 47 people. Ascites was found in 11 of the patients (23.4%). Comorbidity of chronic heart failure (CHF) was found in 31 subjects, 11 of whom had ascites and had a significant correlation [$p = 0.006$; LR 10,823]. There was an increased risk of ascites in subjects with hypoalbuminemia and an SGA score that indicated malnutrition [$p < 0,001$; LR 22,082 dan $p < 0,001$; LR 51,147], respectively. Gender, age, diabetes, hemoglobin, serum creatinine, urea, albumin, hematocrit, and leukocyte levels had no effect on the occurrence of ascites in CKD patients.

Conclusion. Factors related to the incidence of ascites in chronic kidney disease patients undergoing hemodialysis are chronic heart failure, hypoalbuminemia, and SGA score.

INTRODUCTION

Chronic kidney disease (CKD) is a kidney function and structure abnormality in which the glomerular filtration rate is less than 60 mL/min/1.73 m² and kidney damage lasts more than 3 months. This kidney damage is characterized by albuminuria where the albumin excretion rate is ≥ 30 mg/24 hours or urine albumin-creatinine ratio ≥ 30 mg/mmol, abnormal urine sediment, electrolyte disturbances and other abnormalities.¹ Chronic kidney disease is irreversible and progresses slowly and gradually. The disease progresses from chronic to terminal stage in about 2-3 months, but it can take up to 30-40 years. The leading cause of CKD is hypertension (36%), followed by diabetic nephropathy (28%).² Chronic kidney disease,

which has a wide and complex etiology, is still a problem in the field of nephrology. As the population ages, so does the prevalence and incidence of renal failure.²

Nephrogenic ascites, also known as dialysis-related ascites, is a rare condition that can occur in patients with end-stage renal disease (ESRD) who have undergone long-term haemodialysis. It is distinguished by rapid and frequently recurring fluid accumulation and is resistant to conventional management. The prognosis of nephrogenic ascites is generally poor. Renal transplantation is the only definitive treatment for this clinical disease, but the majority of patients with nephrogenic ascites are not considered transplant candidates.³

The first report of nephrogenic ascites in chronic



kidney disease patients undergoing haemodialysis was in 1970. However, the pathogenesis of ascites is still unknown. Ascites is caused by a variety of factors and etiologies. Ascites in CKD patients remains a difficult clinical and therapeutic diagnosis. As a result, early detection of the aetiology or causative factors associated with CKD ascites can aid in the initiation of specific and effective treatment, resulting in better outcomes. However, research on the aetiology and factors associated with ascites in CKD is still lacking, particularly in Indonesia.⁴ Therefore, in this study, the author attempted to identify the various aetiologies and factors that contribute to nephrogenic ascites in patients with advanced or end-stage CKD.

METHOD

This study was an analytical observational study with a cross-sectional approach. This study analyze the factors or etiologies that contribute to the occurrence of nephrogenic ascites in CKD patients receiving haemodialysis. The study was conducted at North Lombok Hospital from September to November 2023, with permission from the Health Research Ethics Committee of the North Lombok Hospital. The total sampling method was used to select the research subjects. The population in this study were end-stage CKD patients undergoing haemodialysis in the haemodialysis unit of North Lombok Hospital. Subjects were obtained from the population who fulfilled the inclusion criteria, including: 1) patients over 18 years old; 2) diagnosed with stage 5 CKD; and 3) undergoing haemodialysis therapy for ≥ 3 months. Meanwhile, the exclusion criteria in this study included: 1) patients with comorbid malignancy or cancer; 2) patients with hepatic cirrhosis; 3) patients with hepatitis B; 4) patients with hepatitis C; and 5) patients with diseases other than CKD. In this study, stage 5 CKD is defined as an abnormality of kidney structure or function with implications for individual health, defined as evidence of kidney damage characterised by a glomerular filtration rate (LFG) < 15 ml/min per 1.73 m² for more than three months, regardless of the cause. Regardless of the cause, 15 ml/min per 1.73 m² for more than three months. The measurement tool was the patient's medical record, and the scale was

nominal.

Ascites is a condition characterized by pathological fluid accumulation in the abdominal cavity. The condition of ascites was determined in this study based on the results of a physical examination and an ultrasound examination performed by a Radiologist. The occurrence of ascites has a nominal scale and is expressed as ascites or not ascites. Furthermore, the collected data was analyzed univariately and bivariately. Univariate analysis was used to examine subject characteristics such as gender, age, and factors or etiology of ascites occurrence seen in patients with comorbid diabetes mellitus (DM) and chronic heart failure (CHF). The most recent laboratory examination results, which included haemoglobin, creatinine, ureum, albumin, haematocrit, and leucocytes, were obtained from the patient's medical records. The SGA (Subjective Global Assessment) score was also examined. Secondary data were obtained from the sample's medical records. If the data was normally distributed, bivariate analysis for categorical data was performed using the Chi Square test. SPSS version 23.0 for Windows was used for statistical tests. Statistical significance was defined as a *p* value of < 0.05 .

RESULTS

Based on research data that has been obtained at North Lombok Hospital regarding factors associated with the incidence of ascites in end-stage CKD patients by searching secondary data, 47 patients were obtained who met the research criteria. Based on physical examination and ultrasound findings, 10 of the 47 patients (21.3%) had ascites. According to sociodemographic characteristics, the majority of the subjects (53.2%) were female and under the age of 65 (93.6%). There were 20 subjects (42.6%) with mild hypoalbuminemia, which is highly associated with fluid overload in CKD patients. Table 1 shows the complete subject characteristics. The results of the analysis of the relationship between the characteristics of the study subjects, comorbid conditions, laboratory results, and SGA scores with the incidence of ascites can be seen in Table 2.

**Table 1. Sociodemographic, clinical, and laboratory characteristics of the study subject**

Variable	Frequency, (n %)
Sex	
Male	22 (46,8)
Female	25 (53,2)
Age	
< 65 years old	44 (93,6)
≥ 65 years old	3 (6,4)
Diabetes mellitus	
Yes	4 (8,5)
No	43 (91,5)
Ascites	
Yes	11 (23,4)
No	36 (76,6)
Chronic heart failure	
Yes	31 (66)
No	16 (34)
Haemoglobin	
≥ 8 g/dl	27 (57,4)
< 8 g/dl	20 (42,6)
Haematocrit	
≥ 30%	9 (19,1)
< 30%	38 (80,9)
Creatinine	
≥ 9 mg/dl	23 (48,9)
< 9 mg/dl	24 (51,1)
Ureum	
≥ 100 mg/dl	37 (78,7)
< 100 mg/dl	10 (21,3)
Hypoalbuminemia	
Mild (< 3,5 g/dl)	20 (42,6)
None (≥ 3,5 g/dl)	27 (57,4)
Leukocytosis/Leukopenia	
Yes	7 (14,9)
No	40 (85,1)
SGA Score	
Moderate mild malnutrition	36 (76,6)
Severe malnutrition	11 (23,4)

Table 2. Analysis of the correlation between characteristics, comorbid conditions, and laboratory results of the study subject with the incidence of nephrosites or nephrogenic ascites

Characteristics	Ascites (n)	No Ascites (n)	P Value	LR (Likelihood Ratio)
Sex				
Male	7	15	0,098	2,786
Female	3	22		
Age				
< 65 years old	10	34	0,352	1,490
≥ 65 years old	0	3		
Diabetes mellitus				



Yes	1	3	0,849	0.035
No	9	34		
Chronic heart failure				
Yes	11	20	0,00*	10.823
No	0	16		
Haemoglobin				
≥ 8 g/dl	5	22	0,591	0,286
< 8 g/dl	5	15		
Haematocrit				
≥ 30%	4	5	0,059	3,141
< 30%	6	32		
Creatinine				
≥ 9 mg/dl	7	16	0,133	2,302
< 9 mg/dl	3	21		
Ureum				
≥ 100 mg/dl	9	28	0,326	1,098
< 100 mg/dl	1	9		
Hypoalbuminemia				
Yes (Mild)	11	10	<0,001*	22,082
No	0	26		
Leukocytosis/Leukopenia				
Yes	2	5	0,630	0,246
No	8	32		
SGA Score				
Moderate mild malnutrition	0	36	<0,001*	51.147
Severe malnutrition	11	0		

DISCUSSION

Based on sociodemographic characteristics, the majority of the study subjects were female. The p value = 0.098 was obtained after analyzing gender and ascites incidence (Table 2), indicating that there was no significant difference in ascites incidence between men and women. According to research by Bindu et al., ascites is more common in women than in men.⁵ Whereas in a study conducted by Yusman et al. and Tasneem et al., it was found that the incidence of ascites was more common in men than women.^{6,7}

A total of 93.6% of the study subjects were less than 65 years old, and after analysis between age and the incidence of ascites, a p value = 0.352 was obtained, indicating that there was no significant difference in the incidence of ascites between the

age groups <65 years and ≥65 years. According to the findings of Tasneem et al. Ascites is more common among people over the age of <40.⁷ Bindu, et al. in their study mentioned that the incidence of ascites is more common in the age group of 40-50 years.⁵ While in a study by Sasanka et al. the mean age of patients suffering from nephrogenic ascites was 36.75 ± 10.12 years.⁸ According to the data, ascites was found in 10 (21.3%) of the study subjects. Furthermore, several factors that may be associated with the incidence of nephroascites in patients with chronic kidney disease were investigated. According to the data, 31 (66%) of the subjects had comorbid CHF, with 11 having ascites manifestations. The statistical test results found a significant correlation (p = 0.00) between CHF and the occurrence of ascites, with a likelihood ratio of 10,823. According to the data,



patients with comorbid CHF are 10.823 times more likely to develop nephroasites than patients without the comorbid condition. As known before, many factors are considered to contribute to the pathogenesis of nephrogenic ascites. Malnutrition and hypoalbuminemia are considered to play a significant role. However, in addition, chronic heart failure is also associated with the development of ascites in CKD patients.³ Cardiovascular disease causes low cardiac output for an extended period of time, resulting in hypotension and hypoperfusion (reduced flow), which activates the system in the kidneys to retain water and salt, resulting in micro and macrovascular damage and renal congestion. Because the flow is disrupted, this will eventually interfere with kidney function and lead to kidney failure.⁹ Chronic heart failure is a condition in which the heart works less efficiently (heart failure) and is accompanied by blockages in various organs of the body, which can result in ascites. Hepatic venous hydrostatic pressure, fluid retention, increased permeability of the peritoneal membrane, and impaired peritoneal lymphatic drainage are all thought to play a role in the development of ascites.¹⁰ Ascites is actually more common in patients with hepatic malfunction, which can lead to cardio-hepatic syndrome or even cardio-renal syndrome.^{11,12} The results of this study are in line with research conducted by Yusman et al., where the incidence of ascites is significantly associated with the incidence of CHF.⁶

In this study, DM risk factors for ascites incidence were also analysed, of which 4 CKD patients (8.5%) had DM etiology. The Chi Square test between diabetes and ascites incidence yielded a p value of 0.849 (Table 2). With a p value > 0.05, there was no significant difference in the incidence of ascites between patients with and without diabetes. This finding contradicts the findings of Elkrief et al, who found that the incidence of diabetes is significantly associated with ascites and renal dysfunction.¹³

Furthermore, the researchers conducted an investigation into the relationship between CKD patients' laboratory examination results and the occurrence of ascites. The relationship between haemoglobin, ureum, serum creatinine, albumin,

hematocrit, and leukocytes was tested in the laboratory. According to the findings of laboratory tests, research subjects with hypoalbuminemia had a significant relationship with the incidence of ascites ($p = <0.001$), with a likelihood ratio of 22.082. A decrease in serum albumin concentration in CKD is frequently a manifestation of protein-energy wasting, a state characterized by metabolic and nutritional changes that result in decreased protein and energy stores. The progression of CKD to renal failure and the initiation of haemodialysis affects a population that is already at risk of hypoalbuminemia, with approximately 60% of patients undergoing haemodialysis having albumin concentrations <4.0 g/dl. One of the causes of hypoalbuminemia appears to be albumin loss into the dialysate via the dialyser.¹⁴ In patients with chronic renal failure, albumin levels can fall (hypoalbuminemia). Albumin is a dispersed protein fraction in the body that functions to maintain plasma osmotic pressure so that ascites does not occur; however, ascites can occur when hypoalbuminemia occurs due to CKD.¹⁵ The results of this study are in line with research conducted by Yusman et al, where it was found that hypoalbuminemia had a significant relationship with the incidence of ascites ($p < 0.001$).⁶ Hypoalbuminemia was also found to contribute to ascites in previous studies by Han et al. and Tasneem et al, which was said to be caused by the patient's poor nutritional condition as the effects of uremia caused anorexia and nausea which ultimately impacted albumin levels.^{7,16}

The laboratory examination results revealed that haemoglobin levels (anaemia) were not related to ascites. The pathogenesis of anaemia in CKD is multifactorial, with impaired EPO (erythropoietin) production thought to be the primary cause. Due to the loss of 1-3 grams of iron per year due to retained blood in the dialyser and repeated blood draws, CKD patients undergoing HD will have a negative iron balance.¹⁷ Based on a study by Yusman et al, the mean haemoglobin levels of CKD patients who experienced ascites and those who did not experience ascites did not have a significant difference ($p > 0.05$).⁶ Similarly, a case report by Abdalla et al in a patient with nephrogenic ascites had a low haemoglobin value of 7.8 g/dl and was



categorised as anaemic.³

Ureum, serum creatinine, haematocrit, and leucocyte levels were not associated with ascites in CKD in this study. If the kidneys fail, it will cause problems. Unused metabolic products such as creatinine and ureum will rise if kidney function declines, which is characterized by a decrease in the ability of the kidneys to excrete urea as well as a decrease in the ability of the glomerulus to perform filtration, resulting in ureum accumulation in the patient's blood. As with ureum, a disruption or decrease in kidney function will result in a buildup of creatinine in the body.^{18,19} Haemodialysis can reduce the accumulation of ureum and creatinine in the blood. Haemodialysis is effective when the ureum-creatinine ratio is reduced. Haksara et al found a significant relationship between dialysis dose settings and a decrease in the incidence of ascites in CKD patients undergoing haemodialysis, demonstrating that the more frequent haemodialysis, the less fluid in the abdominal cavity or ascites that occurred.²⁰ Based on a previous study by Spandana et al, patients with ascites have higher creatinine and ureum values compared to normal people.⁴ Yusman et al. found the same thing, reporting that there was no significant relationship between creatinine and urea levels and ascites in CKD patients.⁶

The results of the hematocrit examination did not show a statistically significant relationship between the percentage of hematocrit and the incidence of ascites. When the number of erythrocytes increases or the amount of plasma volume decreases, haematocrit rises. When there is an increase in plasma volume and a decrease in erythropoiesis or an increase in erythrocyte destruction or loss, haematocrit decreases.²¹ This finding is in a line with the findings of Yusman et al, who found that haematocrit levels had no significant relationship with the occurrence of ascites.⁶

Another study looked at the relationship between leukocyte levels and the occurrence of ascites. The statistical tests revealed that leucocyte levels were not associated with the occurrence of ascites in CKD patients ($p = 0.63$). This finding is in a line with the findings of Yusman et al, who found that

leucocyte levels had no statistically significant relationship with the occurrence of ascites.⁶ In a study conducted by Han et al, nephrogenic ascites was shown to have a low leucocyte count.¹⁶ In addition, in a study conducted by Tasneem et al, it was found that around 53.5% of patients with nephrogenic ascites had a leucocyte count of less than 500/mm³.⁷

Another study looked into the relationship between SGA score (malnutrition vs normal) and ascites incidence. SGA score (malnutrition) was found to be a factor associated with the incidence of ascites in CKD patients ($p < 0.05$). Malnutrition may occur in ascites patients due to insufficient food intake, impaired digestion and absorption, and changes in nutrient metabolism.²² In a study by Perez-Reyes et al, malnourished patients according to SGA had a higher incidence of ascites and a statistically significant association ($p=0.01$).²³ Furthermore, it is well known that CKD patients require haemodialysis (HD), and HD patients are at risk of malnutrition due to restricted protein intake and increased energy use. Malnutrition in CKD patients can cause hypoalbuminemia, which can progress to ascites.²⁴

This study has the advantage of being a relatively quick, cheap, and simple research to conduct because it only uses data sources from records and direct examinations, and multiple factors or causes can be studied directly at the same time, where this study analyzes many factors related to the incidence of ascites in CKD patients such as age, albumin levels, Hb, leukocytes, SGA scores, and others. There were some limitations to this study, such as no examination of dialysis adequacy or dialysis schedule and dose, serum ascites examination albumin gradient (SAAG). This study also found that there is no correlation between the length of time a patient was on haemodialysis and the occurrence of ascites.

CONCLUSION

The findings of this study indicate that chronic heart failure, hypoalbuminemia, and SGA score are factors associated with the occurrence of ascites in CKD patients. Patients with CKD may experience



a decrease in albumin levels (hypoalbuminemia). Hypoalbuminemia in CKD patients can be caused by a variety of factors, including malnutrition due to anorexia and protein restriction. Albumin maintains plasma osmotic pressure, preventing ascites, and ascites can occur with hypoalbuminemia caused by CKD. Chronic heart failure is a condition in which the heart works less efficiently (heart failure) and is accompanied by blockages in other organs, which can lead to ascites. However, further research related to other parameters such as other comorbid conditions, duration of dialysis, and intensity of hemodialysis needs to be done to determine the causative factors of ascites in CKD patients in more detail.

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