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RESEARCH ARTICLE

Correlation between Duration of Hemodialysis and Pleural Effusion Based on Chest X-Ray

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Abstract

Background: Hemodialysis is believed to increase life expectancy and reduce clinical problems experienced by chronic kidney disease (CKD) patients, but various acute and chronic complications can be found in several organ systems, namely in the thoracic and extra thoracic parts of the patient. One of the most common complications is pleural effusion. Thus, we investigated the relationship between duration of hemodialysis and pleural effusion in CKD patients by assessing chest X-ray as initial diagnostic imaging of suspected pleural effusion.

Methods: A cross sectional study was conducted on subjects with CKD underwent routine hemodialysis at Dr. Moewardi General Hospital Surakarta. A total of 100 samples of CKD patients were taken consisted of 50 patients with pleural effusion and 50 patients without pleural effusion. Pleural effusion is confirmed using chest X-Ray. Duration of HD is classified into > 3 months and ≤ 3months. Data analysis was performed using chi square, independent t-test and p value < 0.05 were considered significant.

Results: The duration of hemodialysis was significantly correlated to the incidence of pleural effusion ($p < 0.05$). The proportion of patients who had undergone hemodialysis therapy for more than 3 months was more prevalent in patients with pleural effusion than in patients without pleural effusion (OR = 3.43 CI = 95%).

Conclusions: The duration of hemodialysis was correlated with incidence of pleural effusion. Patients who received HD for more than 3 months was associated with higher risk of pleural effusion in end-stage CKD patients.

Keywords: Hemodialysis; Pleural Effusion; Chest X-ray; Chronic Kidney Disease

Introduction

Chronic Kidney disease (CKD) has become a global burden disease for years and has been widely investigated through times. CKD is a general term use to define clinicopathologic state potentially leading to end-stage renal disease (ESRD), classified into five stages of disease depend on decreased glomerular filtration rate (GFR) starts from <60 mL/min/1.73 m^2 that persist ≥ 3 months [1,2]. Epidemiology study of CKD estimated global CKD prevalence between 11 to 13%. The number is predicted to increase as well as its mortality rate [3].

End-stage CKD with GFR < 15 mL/min/1.73 m^2 demand renal replacement therapy (RRT) to maintain kidney function as regulator of blood pressure, electrolyte balance, and wastes excretion [4,5]. Hemodialysis (HD) is the most common used RRT modality worldwide. HD is one of effective method to improve clinical outcome and quality of life in CKD patients [5,6]. Despite many benefits of HD, there are several complications occur following the treatment such as nausea, vomiting, lethargy, peripheral edema, phlebitis and confusion [5,7,8]. A condition commonly encountered in patients with CKD undergoing hemodialysis is pleural effusion [9]. It is reported that symptomatic pleural effusion is present approximately 7% in CKD patients [10].

The presence of pleural effusion in patients with CKD is usually diagnosed through experienced clinical manifestation and confirmed by radiology imaging using chest X-Ray. Pleural effusion in CKD patients has numerous etiologies and were explained in various pathophysiological mechanisms such as risk of infection, heart failure, pulmonary embolization, autoimmune disease, and

inadequate hemodialysis status [11,12]. This study aimed to investigate the correlation between the duration of hemodialysis and pleural effusion assessed by chest X-ray.

Methods

Data collection

A cross sectional study was conducted in Dr. Moewardi General Hospital, Surakarta Indonesia from June to July 2018. The subjects were patients diagnosed with end-stage CKD underwent routine hemodialysis and chest X-ray follow up. Patients with a history of comorbidities which correlated to develop pleural effusions such as malignancy, heart failure and chronic pulmonary infection or other infections which last for more than 3 months were excluded from the study. Sample consisted of 100 patients divided into two groups, 50 patients with pleural effusion and 50 patients without pleural effusion (control-group). The procedures performed in this present study informed human participants and was approved by the Health Research Ethics Committee Dr. Moewardi General Hospital Surakarta based on Declaration of Helsinki 1975 and its later amendments or comparable ethical standards. After research protocol was obtained, informed consent was collected from a participant who was willing to contribute in this study.

Pleural effusion was determined based on the assessment of chest X-ray in patients by two assessors who had tested reliability or consistency between the two according to the Cohen Kappa agreement test. The duration of hemodialysis was categorized into > 3 months and ≤ 3 months to differentiate and ensure the incidence of CKD from acute kidney injury (AKI).

Other characteristics were also observed such as age, sex, infection, underlying diseases like hypertension, diabetes mellitus, and obstructive uropathy, as well as laboratory examination results such as hemoglobin, creatinine, and estimated glomerular filtration rate (eGFR). Nominal variables were described with numbers of frequencies and percentages, while numerical variables were described as mean and standard deviations.

Data analysis

The difference in nominal variables between the two samples according to pleural effusion was analyzed with chi square test. The relationship between the duration of hemodialysis and the characteristics of patients with pleural effusion was conducted by multivariate logistic regression models. Significant p values lower than 0.05 were considered (95% confidence interval [CI]). The data processing was conducted using SPSS for Windows 17.0 computer program.

Results

The average age of patients observed was 48.96 ± 12.81 years consisting of 56 patients (56%) men and 44 patients (44%) women. The assessment of CKD underlying disease found that hypertension was present in 79 patients (79%), followed by diabetes mellitus (DM) in 27 patients (27%), and obstructive uropathy in 3 patients (3%). Of the 100 patients, 63 were on routine hemodialysis for more than 3 months. Clinical feature, laboratory results particularly anemic status and kidney function were assessed in this study. The demographic, clinical, laboratory and etiology characteristics of the study subjects were presented in Table 1.

Characteristics	Frequency (%)	Mean±SD
Age (years)		48.96 ± 12.81
Sex **Male** **Female**	 56 (56.0) 44 (44.0)	
Acute Infection **Yes** **No**	 15 (15.0) 85 (85.0)	
Edema **Yes** **No**	 74 (74.0) 26 (26.0)	
Hypertension **Yes** **No**	 79 (79.0) 21 (21.0)	
Diabetes mellitus **Yes** **No**	 27 (27.0) 73 (73.0)	
Obstructive Uropathy **Yes** **No**	 3 (3.0) 97 (97.0)	
Hemoglobin (g/dl)		9.34 ± 7.76
Serum creatinine (mg/dl)		10.64 ± 5.06
eGFR (ml/min/1.73m^2)		5.76 ± 3.14

Characteristics	Frequency (%)	Mean±SD
Duration of Hemodialysis **> 3 months** **≤ 3 months**	 63 (63.0) 37 (37.0)	
Pleural Effusion **Yes** **No**	 50 (50.0) 50 (50.0)	
Pleural Effusion site* **Bilateral** **Right** **Left**	 32 (64.0) 14 (28.0) 4 (8.0)	

Table 1: Demographic, clinical, laboratory and etiology characteristics of patients

Pleural effusions in subjects were confirmed by two radiology imaging assessor using Kappa Cohen contingency test. The result of pleural effusion incidence is found in half of subjects with bilateral effusion (64%) is the most common feature in patients, followed by right hemithorax pleural effusion (14%) and left hemithorax pleural effusion (8%).

The comparison of patient characteristics and duration of HD between patients with pleural effusion and without pleural effusion, seen in Table 2. The result of this study found that proportion of patients who experienced pleural effusion (76%) is more prevalent in the group of patients who had received HD for ≥ 3 months ($p < 0.05$). There were also other three characteristics valued or distribution differ significantly based on the incidence of pleural effusion namely edema ($p < 0.05$), hypertension ($p < 0.05$) and eGFR levels ($p < 0.05$). These results explained that patients with edema manifestation were more risky to develop pleural effusion and the more severe renal impairment also contributed in greater risk for pleural effusion.

Characteristics	**Pleural Effusion** (n = 50)	**Non Pleural Effusion** (n = 50)	P value
Age (years)	47.68 ± 11.60	50.24 ± 13.92	0.320
Sex **Male** **Female**	 28 (56.0) 22 (44.0)	 28 (56.0) 22 (44.0)	1.000
Infection **Yes** **No**	 8 (16.0) 42 (84.0)	 7 (14.0) 43 (86.0)	0.779
Edema **Yes** **No**	 45 (90.0) 5 (10..0)	 29 (58.0) 21 (42.0)	< 0.001*
Hypertension **Yes** **No**	 44 (88.0) 6 (12.0)	 35 (70.0) 15 (30.0)	0.027*
Diabetes mellitus **Yes** **No**	 11 (22.0) 39 (78.0)	 16 (32.0) 34 (68.0)	0.260
Obstructive Uropathy **Yes** **No**	 1 (2.0) 49 (98.0)	 2 (4.0) 48 (96.0)	0.558
Hemoglobin (g/dl)	10.02 ± 10.83	8.66 ± 1.84	0.383
Serum creatinine (mg/dl)	11.39 ± 4.91	9.88 ± 5.15	0.138
eGFR (ml/min/1.73m²)	5.14 ± 2.56	6.38 ± 3.55	0.048*
Duration of Hemodialysis **> 3 months** **≤ 3 months**	38 (76.0) 12 (24.0)	25 (50.0) 25 (50.0)	0.007*

Table 2: Correlation between patient characteristic and pleural effusion occurrence in HD patients

Variable	p	OR	95% CI	
			Lower	Upper
Duration of Hemodialysis (> 3 months)	0.01*	2.506	0.959	6.547
Edema (Yes)	0.002*	6.048	1.964	18.628
Hypertension (Yes)	0.474	1.552	0.466	5.171
eGFR (ml/min/1.73m²)	0.278	0.918	0.788	1.071

Table 3: Correlation between duration of HD, edema, hypertension, eGFR and pleural effusion

We found that patients with pleural effusion had a prevalence of edema and hypertension as well as lowered eGFR level. The duration of hemodialysis, edema, hypertension, and eGFR levels, were then analyzed in *chi square* analysis (Table 3). In the

multiple logistic regression model, the duration of hemodialysis was only marginal with the incidence of edema, hypertension and lowered eGFR (p = 0.061; OR = 2.506; 95% CI = 0.959 - 6.547). The result in this study presented in Table 3.

Discussion

Hemodialysis (HD) is a form of renal replacement therapy (RRT) used as a treatment modality for end-stage CKD patients. The target of this therapy is to replace the damaged excretory function of the kidney by restoring the conditions of intracellular and extracellular fluids under normal conditions [6,13]. There are several complications occur following this therapy. Acute complications in HD may present when the dialysis process has just begun, such as cardiovascular complications, electrolyte imbalance, nausea, vomiting, pruritus, neurological, and hematological, dysfunction [5,7].

Transudative pleural effusion is more prevalent in patients undergoing HD, with congestive heart failure being the most common cause [11]. In a previous study, 20% of patients on long-term HD developed pleural effusion [14]. Pleural effusion associated with left ventricular failure often causes transudative or bilateral pleural effusion, where the fluid originates from pulmonary interstitial passes through the visceral pleura and then start to accumulate in the pleural cavity [15].

If HD patients do not have adequate ultrafiltration, it could conduct to excessive fluid accumulation (approximately 6-7% of the body dry weight) in the period between hemodialysis sessions [16]. Chronic accumulation of excessed body fluid volume in patients undergoing HD may directly impact on hypertension, increased arterial stiffness, left ventricular hypertrophy, heart failure, and increase the mortality and morbidity of patients [17,18]. Long-term dialysis patients periodically have increased mean concentration of NT-proBNP and cTnT, whereas those are accurate and sensitive markers to evaluate heart failure and ischemic heart damage [18-20].

Other predisposing factors resulting in pleural effusion in CKD patients undergoing HD are alleviated immune status, hyperuremic conditions, malnutrition, DM, and long-term corticosteroid uses [11,12]. Uremia leads to interference with cellular immunity which is the arch defense mechanism against infections especially secondary tuberculosis which is documented risk of TB infection are 6 to 25 times more likely develop in CKD patients undergoing chronic dialysis. Tuberculosis induced long-term dialysis may also associate in pleural effusion [21,22]. It is also reported in recent study that DM is a predictor of the occurrence of pleural effusion associated with altered capillary permeability, decreased immune response, disruption of neutrophils and macrophage functions [18,23].

In this study the duration of hemodialysis was significantly associated with the incidence of pleural effusion. Presenting edema and decreased eGFR in patients also aggravated the risk of pleural effusion development due to weakened kidney function to maintain fluid balance. However, the infirmity of this study is control in fluid balance was not done intensively in this study and it can lead to research bias. Moreover, the mean of hemoglobin in both groups were low, since the patients were not given anemia treatment, it can also associate with pleural effusion. In addition, differences in management that have been given to patients and patient lifestyle factors may also influence the incidence of pleural effusion. The findings may also differ from one study to another depending on the method of determining pleural effusion and the long-term cutoff determination of hemodialysis.

Conclusion

It is concluded in this study that there is significant correlation between duration of hemodialysis (HD) and pleural effusion in patients with end-stage CKD. This study also found that patients who already receive HD more than 3 months have greater risk experiencing pleural effusion. Adequacy of the treatment and monitoring of this therapy are important to prevent future complication following HD procedure. Therefore, further investigation of other complications related to HD is helpful to assess HD efficiency as renal replacement therapy.

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