ORIGINAL ARTICLE

Comparison of Pulmonary Arterial Hypertension and Risk Factors in End Stage Renal Disease Patients with Peritoneal Dialysis and Hemodialysis

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Background: Pulmonary arterial hypertension (PAH) is associated with high mortality and frequent complications in end stage renal disease patients. Epidemiological data for this disorder across the spectrum of end stage renal disease in Thai patients is limited.

Objective: To compare the prevalence and risk factors of PAH in hemodialysis and peritoneal dialysis in end stage renal disease among the Thai patients.

Materials and Methods: The authors retrospectively studied in patients with end stage renal disease at Pranangklao Hospital between January 2016 and December 2021.

Results: A total of 201 patients were enrolled. The average age of patients was 55.57±16.22 years (47.3% male). Most patients had hypertension. Most patients had been prescribed folic acid. The number of patients with mean pulmonary artery pressure >20 mmHg was 81 (77.1%) in the hemodialysis group and 52 (54.2%) in the peritoneal dialysis group (p<0.001). PAH in hemodialysis was higher than peritoneal dialysis (OR 2.86, 95% CI 1.56 to 5.24, p<0.001). The following were factors associated with PAH: history of coronary artery disease (OR 2.77, 95% CI 1.29 to 5.94, p<0.009), history of beta-blocker use (OR 2.09, 95% CI 1.15 to 3.79, p<0.015), left ventricular ejection fraction by Simpson's method (OR 0.95, 95% CI 0.92 to 0.98, p<0.001). The variable associated with PAH (peritoneal dialysis group) in multivariate logistic regression was Hemodialysis (adjusted OR 3.16, 95% CI 1.66 to 6.03, p<0.001).

Conclusion: End stage renal disease in Thai patients undergoing hemodialysis carry a three-fold risk of pulmonary hypertension than peritoneal dialysis patients.

Keywords: Pulmonary hypertension; Hemodialysis; Peritoneal dialysis

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Chronic kidney disease is a common progressive disease classified by its pathophysiology with a mechanism which is caused by abnormal kidney function or structural changes that have continued for at least three months. Chronic kidney disease is classified in stages according to its glomerular filtration rate (GFR), for example, at stage 5 GFR <15 mL/minute/1.73 m^2[1].

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Cardiovascular complications are the most common cause of death in end stage renal disease[2,3]. Pulmonary arterial hypertension, a subset of cardiovascular complications, is one of the deadliest causes. More importantly, pulmonary arterial hypertension is associated with a significantly increased risk of hospitalization and death in chronic kidney disease patients[4-6].

The gold standard for diagnosing pulmonary arterial hypertension is right heart catheterization to measure pressure in the right heart, however, this method is costly and carries a high risk. Echocardiography is an alternative diagnostic option for pulmonary arterial hypertension, with 83% sensitivity and 72.4% specificity. Hypertensive pulmonary artery was defined as systolic-pressure pulmonary artery ligature greater than 20 mmHg at rest as measured by echocardiography[7,8].

The prevalence of pulmonary arterial hypertension in end stage renal disease patients ranged

from 9% to 39% in those with end stage renal disease, between 18.8% to 68.8% in hemodialysis patients, and between 0% and 42% in peritoneal dialysis patients[9]. Multiple mechanisms affect the incidence of pulmonary arterial hypertension in various kidney diseases such as left ventricular dysfunction, endothelial vessel dysfunction, and atherosclerosis[10].

The goal of the present study was to examine the prevalence of pulmonary arterial hypertension and its risk factors in end stage renal disease patients undergoing peritoneal dialysis and hemodialysis in Thai population.

Materials and Methods

The present study was conducted retrospectively in Pranangklao Hospital (PE6529, EC35/2565) between January 1, 2016 and December 31, 2021. Patients ≥18 years old diagnosed with end stage renal disease with peritoneal dialysis and hemodialysis were enrolled. All the patients received echocardiography. The following patients were excluded: 1) patients with a history of cardiac arrhythmia, 2) patients with a history of metallic valve replacement surgery, and 3) patients with a history of significant valvular dysfunction. The sample size was estimated to be 36, based on the infinite population mean calculation technique. Using previous data[11] by Reid et al. the standard deviation and error approximates were 17 and 3, respectively, Type I & II errors were predetermined at 0.05 and 0.2, respectively.

The present study protocol was approved by the Institutional Review Board No. PE6530 and is in compliance with the Declaration of Helsinki, CIOMS Guidelines and International Conference on Harmonization in Good Clinical Practice (ICH-GCP).

Statistical analysis

Descriptive statistics, including frequency and percentages, were used for categorical variables. Continuous variables were reported as mean and standard deviation (SD). The distribution of variables was examined by the Kolmogorov-Smirnov test. The ANOVA test and chi-square test were used for comparison of normally and continuously distributed categorical data respectively. A p-value of less than 0.05 was considered statistically significant. Comparison of pulmonary arterial hypertension and risk factors in end stage renal disease patients with peritoneal dialysis and hemodialysis used Logistic regression and Pearson's correlation. The IBM SPSS Statistics, version 26.0 (IBM Corp., Armonk, NY, USA) was used to perform all statistical analyses.

Results

According to the Pranangklao Hospital database, 201 patients were diagnosed with end stage renal disease between January 1, 2016 and December 31, 2021.

Baseline characteristics were shown in Table 1. Ninety-six patients had peritoneal dialysis and one hundred five had hemodialysis. For patients who had peritoneal dialysis, the average age was 55.57±16.22 years and 55 (53.1%) were male. In those who had hemodialysis, the average age was 58.23±14.16 years and 44 (41.9%) were male. Most patients had hypertension in both the peritoneal and hemodialysis groups, 94 (97.9%) and 103 (98.1%), respectively. Most patients had been prescribed folic acid 77 (80.2%) in the peritoneal group 94 (89.5%) and the hemodialysis group. Left ventricular ejection fraction by the Simpson's method was 58.89±12.57% in the peritoneal group and 59.79±12.95% in the hemodialysis group. The data for baseline characteristics of both groups showed no statistical significance.

Mean pulmonary artery pressure was 25.65±12.38 mmHg and 27.64±10.45 mmHg in the peritoneal and hemodialysis groups, respectively, with no statistical significance. However, the mean pulmonary artery pressure >20 mmHg was 81 (77.1%) in the hemodialysis group and 52 (54.2%) in the peritoneal group with statistical significance ($p<0.001$).

Univariate logistic regression was shown in Table 2. Pulmonary arterial hypertension in hemodialysis was univariately associated with peritoneal dialysis (OR 2.86, 95% CI 1.56 to 5.24, $p<0.001$). History of coronary artery disease (OR 2.77, 95% CI 1.29 to 5.94, $p<0.009$), beta blocker use (OR 2.09, 95% CI 1.15 to 3.79, $p<0.015$), left ventricular ejection fraction by Simpson's method (%) (OR 0.95, 95% CI 0.92 to 0.98, $p<0.001$). Multivariate logistic regression was shown in Table 3. Variables associated with pulmonary arterial hypertension (peritoneal dialysis group) in multivariate logistic regression were known cases of hemodialysis (adjusted OR 3.16, 95% CI 1.66 to 6.03, $p<0.001$).

Discussion

The present study found the prevalence of pulmonary arterial hypertension to be 81 (77.1%) in hemodialysis group and 52 (54.2%) in peritoneal dialysis group of end stage renal disease patients in the Thai population. Previous studies had also reported higher prevalence of pulmonary hypertension in hemodialysis patients[12].

Table 1. Baseline characteristics of the patients

Baseline characteristics	Peritoneal dialysis (n=96)	Hemodialysis (n=105)	p-value
Age (years); mean±SD	55.57±16.22	59.23±14.16	0.090
Male; n (%)	51 (53.1)	44 (41.9)	0.111
Height (cm); mean±SD	161.45±9.06	159.76±9.46	0.199
Weight (kg); mean±SD	59.09±11.47	60.67±13.77	0.382
Body surface area (m^2); mean±SD	1.62±0.17	1.62±0.2	0.869
estimated Glomerular filtration rate (mL/minute/1.73 m^2); mean±SD	6.15±3.18	7.26±2.8	0.009
Hematocrit (%); mean±SD	31.99±4.68	31.8±4.64	0.763
Coronary artery disease; n (%)	26 (27.1)	27 (25.7)	0.826
Hypertension; n (%)	94 (97.9)	103 (98.1)	0.928
Diabetes mellitus; n (%)	55 (57.3)	74 (70.5)	0.051
Dyslipidemia; n (%)	85 (88.5)	100 (95.2)	0.080
Cerebrovascular artery disease; n (%)	5 (5.2)	1 (1.0)	0.077
Chronic obstructive pulmonary disease; n (%)	2 (2.1)	3 (2.9)	0.725
Aspirin; n (%)	47 (49.0)	55 (52.4)	0.628
Clopidogrel; n (%)	18 (18.8)	25 (23.8)	0.382
Betablocker; n (%)	48 (50.0)	59 (56.2)	0.380
Calcium channel blocker; n (%)	59 (61.5)	73 (69.5)	0.229
Angiotensin converting enzyme inhibitor/Angiotensin II receptor blocker; n (%)	33 (34.4)	44 (41.9)	0.273
Aldactone; n (%)	4 (4.2)	1 (1.0)	0.144
Statin; n (%)	77 (80.2)	87 (82.9)	0.628
Furosemia; n (%)	64 (66.7)	66 (62.9)	0.572
Isosorbide mononitrate; n (%)	30 (31.3)	31 (29.5)	0.790
Hydralazine; n (%)	40 (41.7)	31 (29.5)	0.072
Sodium bicarbonate; n (%)	45 (46.9)	49 (46.7)	0.976
Ferrous sulfate; n (%)	54 (56.3)	63 (60.0)	0.590
Folic acid; n (%)	77 (80.2)	94 (89.5)	0.064
Left ventricular Ejection fraction by Simpson's method (%); mean±SD	58.89±12.57	59.79±12.95	0.616
Mean pulmonary artery pressure (mmHg); n (%)			
Mean±SD	25.65±12.38	27.64±10.45	0.219
≤20	44 (45.8)	24 (22.9)	0.001*
>20 (pulmonary hypertension)	52 (54.2)	81 (77.1)	0.001*

SD=standard deviation

Chi-square and independent t-test, * $p<0.05$ is considered statistically significant

There is no clear explanation for the high prevalence of pulmonary arterial hypertension in hemodialysis patients. Many patients with hormonal and metabolic disorders are caused by narrowing of the pulmonary artery[13]. Previous studies concluded that long-term hemodialysis via arteriovenous access may be involved in the pathogenesis of pulmonary hypertension by affecting pulmonary vascular resistance and cardiac output[14].

History of coronary artery disease and beta blocker use was found to be associated with elevated pulmonary artery pressure (pulmonary arterial hypertension) in peritoneal and hemodialysis patients. This finding has not been previously reported in patients undergoing hemodialysis and peritoneal dialysis. A large portion of patients in the present study were found to have pulmonary arterial hypertension through echocardiographic detection of left ventricle ejection fraction measured by the Simpson's method. This is because pulmonary arterial hypertension is a common complication of heart failure[15].

After multivariate logistic regression, the Thai population with end stage renal disease undergoing hemodialysis carries about a three-fold risk of pulmonary arterial hypertension than peritoneal dialysis patients.

There are some limitations to the present study. Firstly, the relatively small sample size of patients with end stage renal disease undergoing

Table 2. Univariate logistic regression: Comparison of pulmonary arterial hypertension and risk factor in end stage renal disease patients with peritoneal dialysis and hemodialysis

Parameter	Mean PAP >20 (n=133)	Mean PAP ≤20 (n=68)	OR (95% CI)	p-value
Peritoneal dialysis; n (%)	52 (39.1)	44 (64.7)	Reference	1
Hemodialysis; n (%)	81 (60.9)	24 (35.3)	2.86 (1.56 to 5.24)	0.001*
Age (years); mean±SD	56.27±14.53	59.84±16.44	0.98 (0.96 to 1)	0.119
Male; n (%)	64 (48.1)	31 (45.6)	1.11 (0.62 to 2)	0.734
Height (cm); mean±SD	161±9.49	159.72±8.87	1.02 (0.98 to 1.05)	0.355
Weight (kg); mean±SD	60.48±13.27	58.81±11.57	1.01 (0.99 to 1.03)	0.378
Body surface area (m^2); mean±SD	1.63±0.19	1.59±0.18	2.89 (0.58 to 14.56)	0.197
estimated Glomerular filtration rate (mL/minute/1.73 m^2)	6.62±2.97	6.93±3.17	0.97 (0.88 to 1.06)	0.503
Hematocrit (%); mean±SD	31.89±4.69	31.89±4.6	1 (0.94 to 1.07)	0.992
Coronary artery disease; n (%)	43 (32.3)	10 (14.7)	2.77 (1.29 to 5.94)	0.009*
Hypertension; n (%)	131 (98.5)	66 (97.1)	1.98 (0.27 to 14.41)	0.498
Diabetes mellitus; n (%)	87 (65.4)	42 (61.8)	1.17 (0.64 to 2.15)	0.61
Dyslipidemia; n (%)	124 (93.2)	61 (89.7)	1.58 (0.56 to 4.45)	0.385
Cerebrovascular artery disease; n (%)	3 (2.3)	3 (4.4)	0.5 (0.1 to 2.55)	0.404
Chronic obstructive pulmonary disease ; n (%)	4 (3.0)	1 (1.5)	2.08 (0.23 to 18.96)	0.517
Aspirin; n (%)	70 (52.6)	32 (47.1)	1.25 (0.7 to 2.24)	0.455
Clopidogrel; n (%)	31 (23.3)	12 (17.6)	1.42 (0.68 to 2.98)	0.356
Beta blocker; n (%)	79 (59.4)	28 (41.2)	2.09 (1.15 to 3.79)	0.015*
Calcium channel blocker; n (%)	89 (66.9)	43 (63.2)	1.18 (0.64 to 2.17)	0.603
Angiotensin converting enzyme inhibitor/angiotensin II receptor blocker; n (%)	48 (36.1)	29 (42.6)	0.76 (0.42 to 1.38)	0.366
Aldactone; n (%)	5 (3.8)	0 (0.0)	N/A	0.999
Statin; n (%)	110 (82.7)	54 (79.4)	1.24 (0.59 to 2.6)	0.569
Furosemide; n (%)	85 (63.9)	45 (66.2)	0.91 (0.49 to 1.67)	0.75
Isosorbide mononitrate; n (%)	46 (34.6)	15 (22.1)	1.87 (0.95 to 3.67)	0.07
Hydralazine; n (%)	52 (39.1)	19 (27.9)	1.66 (0.88 to 3.12)	0.119
Sodium bicarbonate; n (%)	60 (45.1)	34 (50)	0.82 (0.46 to 1.48)	0.511
Ferrous sulfate; n (%)	78 (58.6)	39 (57.4)	1.05 (0.58 to 1.91)	0.86
Folic acid; n (%)	114 (85.7)	57 (83.8)	1.16 (0.52 to 2.6)	0.722
Left ventricular ejection fraction by Simpson's method (%); mean±SD	57.2±14.35	63.58±7.21	0.95 (0.92 to 0.98)	0.001*

SD=standard deviation; PAP=pulmonary artery pressure; OR=odds ratio; CI=confidence interval

* $p<0.05$ is considered statistically significant

Table 3. Adjusted odds ratio, comparison of pulmonary arterial hypertension, and risk factor in end stage renal disease patients with peritoneal dialysis and hemodialysis

	Adjusted OR	95% CI	p-value
Group			
Peritoneal dialysis	Reference	-	1
Hemodialysis	3.16	1.66 to 6.03	<0.001*
Coronary artery disease	1.91	0.82 to 4.42	0.131
Beta blocker	1.85	0.98 to 3.5	0.059
Left ventricular ejection fraction by Simpson's method (%)	0.95	0.92 to 0.99	0.006*

OR=odds ratio; CI=confidence interval

peritoneal dialysis and hemodialysis were available, in addition to the retrospective study design. Secondly, the present study design did not account for other pertinent factors that may contribute to the presence of pulmonary arterial hypertension in these patients, namely the duration of peritoneal dialysis or hemodialysis, and blood pressure. Finally, the study population was recruited from a single center in Thailand which may limit the generalizability of the data. The present study was conducted on a small number of Thai patients, therefore, further studies in the future will consolidate the implications of the present study data.

Conclusion

The prevalence of pulmonary hypertension was high among the end stage renal disease patients

undergoing hemodialysis. History of coronary artery disease, along with beta blocker use and decreased left ventricular systolic ejection fraction were also detected as risk factors for pulmonary arterial hypertension.

What is already known on this topic?

The prevalence of pulmonary arterial hypertension in end stage renal disease patients in the Thai population is higher for those undergoing hemodialysis compared to peritoneal dialysis.

What this study adds?

History of coronary artery disease, along with beta blocker use and decreased left ventricular systolic ejection fraction were the risk factors for pulmonary arterial hypertension in end stage renal disease Thai patients undergoing hemodialysis.

Conflicts of interest

The authors declare no conflicts of interest.

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