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Frequency of Pulmonary Hypertension in Patients with Chronic Kidney Disease Stage 5 (CKD Stage 5) and Correlation of PASP with Biochemical Parameters of CKD

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Abstract **Original Research Article**

Background: Pulmonary hypertension is an independent predictor of mortality. It is a recognized condition in patients with chronic kidney disease. ***Objective:*** To find out the frequency of pulmonary hypertension in CKD stage 5 patients and relation of PASP with biochemical parameters of CKD. ***Methods:*** This cross-sectional study was conducted in the Department of Nephrology at Bangabandhu Sheikh Mujib Medical University, Dhaka from July 2014 to June 2016 over a period of 2(two) years. One hundred twenty patients with CKD stage 5 on dialysis (HD and CAPD) and pre dialysis for more than 3 months were selected for this study. ***Result:*** Pulmonary hypertension was found in 56.6% maintenance HD patients, in 13.3% CAPD patients and in 20.6% pre dialysis patients. A significant correlation of pulmonary arterial systolic pressure with age, duration of dialysis, serum phosphate, and serum iPTH levels was found. ***Conclusion:*** Frequency of pulmonary hypertension was highest in hemodialysis group (56.6%). Routine screening and early detection is important in order to avoid the serious consequences of the disease.

Keywords: pulmonary hypertension**,** chronic kidney disease, PASP.

INTRODUCTION

Chronic kidney disease (CKD) is equally affecting the people of developed countries as well as developing countries. The prevalence of CKD is rapidly increasing globally. In developed countries it is 13% [1]; however, in developing countries, population based studies on the prevalence of CKD are limited [2]. The precise nationwide prevalence of CKD in Bangladesh is still unknown [3]. Data from hospital, urban, and underprivileged population based studies suggest that prevalence of CKD ranges from 16.0 to 18.0% in Bangladesh; of them, 11.0% belongs to stage 3 and above [4].

CKD is recognized as a condition that elevates the risk of cardiovascular complications as well as kidney failure and complications [5]. The complications of CKD are due to the disease itself as well as the mode of renal replacement therapy (RRT). Kidney functions can only be partly replaced by maintenance dialysis, which provides only 5% to 10% of excretory renal function [6]. At present out of three modalities of treatment about 82.0% of patients are on HD [7]. Cardiovascular morbidity and mortality is highest in dialysis populations. Currently an association is found between renal replacement therapy (RRT) and development of pulmonary hypertension (PH) [8].

Pulmonary hypertension (PH) has been traditionally defined as a mean pulmonary artery pressure of at least 25 mm of Hg at rest at with a pulmonary capillary wedge pressure of 15 mm of Hg or less [9]. It is a devastating disorder characterized by

elevated pulmonary artery pressure (PAP) and has been reported as a new entity and an unrecognized threat in a considerable proportion of patients with end stage renal disease (ESRD) [10]. Regardless of the etiology, PH occurs frequently in patients with CKD especially those with CKD stage 5 and dialysis. The prevalence of PH ranges from 9%-39% in individuals with stage 5 CKD, 18.8% to 68.8% in hemodialysis patients, and 0%-42% in patients on peritoneal dialysis therapy [11].

Based on an echocardiographic diagnosis of PH, the prevalence of PH ranges from 9% to 39% in stage 5 CKD patients [12], from 18.8% to 68.8% in hemodialysis patients and from 0% to42% in patients on peritoneal dialysis [13]. The exact mechanisms of PH in this population remain poorly understood. PH might be induced and/or aggravated by left ventricular disorders and risk factors typical of CKD, including volume overload, arteriovenous fistula, sleep disordered breathing, exposure to dialysis membranes, endothelial dysfunction, vascular calcification and stiffening, and severe anemia [9]. Early diagnosis and early intervention of PH might improve the long-term outcomes [14]. Therefore, it is crucial to investigate the epidemiology of PH before CKD patient's progress to ESRD. However, no epidemiological data are available for the earlier stages of CKD. Although a very recent study reported the presence of CKD Stages 3–4 with PH, those patients were selected from a PH registry, and non-PH CKD data were lacking; therefore, the study did not show the actual epidemiology of CKD [15]. Besides, the study revealed a prognostic value of PH in predicting cardiovascular (CV) outcomes in maintenance hemodialysis (MHD) patients [16]; whether there is a link between PH and CV disease in other stages of CKD is unknown. Therefore, the present study was undertaken to see the frequency of pulmonary hypertension in CKD stage 5 patients on dialysis (HD and CAPD) and pre dialysis and relation of PASP with biochemical parameters of CKD.

METHODS

This cross-sectional study was conducted in the Department of Nephrology at Bangabandhu Sheikh Mujib Medical University, Dhaka from July 2014 to June 2016 over a period of 2 (two) years. Sixty-eight adult patients with chronic kidney disease stage 5 and on dialysis (HD, CAPD) and pre dialysis for more than 3 months were enrolled for this study. Patients with chronic obstructive pulmonary disease, diffuse parenchymal lung disease, chest wall disease, cardiovascular disease, uncontrolled arterial hypertension and collagen vascular disease were excluded from this study. After taking written consent age, sex, smoking habits, associated co-morbidities, etiology of renal failure, duration of dialysis treatment, access location of arteriovenous fistula (AVF) brachial or radial were recorded. Laboratory investigations such as hemoglobin, serum creatinine, serum calcium, serum inorganic phosphate, serum intact parathyroid hormone, serum albumin were measured.

Quantitative data were expressed as mean and standard deviation and qualitative data were expressed as frequency distribution and percentage. Statistical analyses were performed by using SPSS-12. Association between categorical variables were analyzed by Chi-Square test and continuous variable by t-test used. Pearson's correlation coefficient was used to test the relationship between pulmonary arterial systolic pressure (PASP) and biochemical parameters (Hemoglobin, serum creatinine, serum calcium, serum inorganic phosphate, serum I.PTH, serum albumin) of chronic kidney disease (CKD). For all statistical tests, we considered p value <0.05 as statistically significant.

RESULTS

Table-I: Frequency of pulmonary hypertension in different treatment groups (n=102)

	With PH	Without PH	P value
Pre dialysis	7 (20.6%)	27 (79.4%)	<0.001
CAPD	2 (13.3%)	13 (86.7%)	
HD	30 (56.6%)	23 (43.4%)	
Total	**38 (37.3%)**	**64 (62.7%)**	

Table I shows that pulmonary hypertension was significantly high in the HD group compared to the other two groups.

Table-II: Gender and age distribution in patients with and without pulmonary hypertension (n=102)

Gender	With PH (n=39)	Without PH (n=63)	P value
Age (years)	48.20 ± 14.05	40.65 ± 10.63	0.003[s]
Gender			
Male	24 (37.5%)	40 (62.5%)	0.387
Female	15 (39.5%)	23 (60.5%)	

Table II shows that 39.5% of females and 37.5% of males had PH. PH was found among aged patients.

Table-III: Duration of dialysis in different treatment groups (n=68)

	Duration of dialysis (months) [Mean ± SD]		p-value
	With PH	Without PH	
CAPD (n=15)	14.5 ± 4.95	4.62 ± 1.26	**<0.001**
HD (n=53)	10.17 ± 6.11	6.74 ± 4.55	**0.029**

Table III shows that patients with pulmonary hypertension in both treatment groups had undergone significantly longer duration of dialysis than those who still did not develop pulmonary hypertension.

Table-IV: HD access in patients with and without pulmonary hypertension (n=53)

	With PH (n=30)	Without PH (n=23)	P value
Radial artery (n=37)	20 (54.1%)	17 (45.9%)	0.569
Brachial artery (n=16)	10 (62.5%)	6 (37.5%)	

Table IV shows number of patients with different sites of HD access with and without pulmonary hypertension. Among 37 patients with radial artery access, 20 (54.1%) had pulmonary hypertension and among 16 patients with brachial artery access, 10 (62.5%) had pulmonary hypertension.

Table-V: Biochemical parameters in patients with and without pulmonary hypertension in different treatment groups (n=102)

Biochemical findings	With PH	Without PH	P value
Serum creatinine (mg/dl)			
Pre dialysis (n=34)	7.07 ± 0.64	6.07 ± 0.96	**0.015**
CAPD (n=15)	7.90 ± 1.84	6.70 ± 1.43	0.303
HD (n=53)	7.25 ± 1.93	6.90 ± 1.12	0.431
Hb (gm/dl)			
Pre dialysis (n=34)	8.73 ± 1.59	8.89 ± 1.50	0.801
CAPD (n=15)	7.20 ± 0.14	10.08 ± 1.81	**0.048**
HD (n=53)	8.87 ± 1.57	9.22 ± 1.84	0.467
Serum Albumin (gm/l)			
Pre dialysis (n=34)	31.00 ± 8.56	34.52 ± 6.39	0.235
CAPD (n=15)	34.00 ± 7.07	29.85 ± 6.66	0.428
HD (n=53)	32.10 ± 3.79	32.96 ± 5.45	0.503
Corrected serum Ca (mmol/l)			
Pre dialysis (n=34)	2.01 ± 0.11	2.41 ± 0.61	0.099
CAPD (n=15)	2.27 ± 0.21	2.19 ± 0.23	0.657
HD (n=53)	2.16 ± 0.28	2.24 ± 0.25	0.316
Serum PO_4 (mmol/l)			
Pre dialysis (n=34)	1.39 ± 0.17	1.36 ± 0.29	0.828
CAPD (n=15)	1.25 ± 0.49	1.37 ± 0.35	0.683
HD (n=53)	1.54 ± 0.36	1.22 ± 0.23	**0.001**
Serum iPTH (pg/ml)			
Pre dialysis (n=34)	433.07 ± 101.84	137.25 ± 80.69	**<0.001**
CAPD (n=15)	219.85 ± 73.33	205.95 ± 140.78	0.896
HD (n=53)	384.56 ± 102.38	101.55 ± 92.54	**0.013**

Table V shows that serum iPTH was significantly higher among pulmonary hypertension patients compared to those without pulmonary hypertension in the HD and pre dialysis groups. Serum creatinine was higher, Hb was lower and serum phosphate was higher in patients with pulmonary hypertension than those of without pulmonary hypertension in the pre dialysis, the CAPD and the HD groups respectively.

Table-VI: Correlation of PASP with different variables in different treatment groups (n=102)

Parameters	Group					
	Pre dialysis (n=34)		CAPD (n=15)		HD (n=53)	
	r value	p value	r value	p value	r value	p value
Age (years)	0.450	**0.008**	0.806	**<0.001**	0.583	**<0.001**
Duration of dialysis (months)			0.689	**0.004**[s]	0.349	**0.010**
Serum creatinine (mg/dl)	0.396	**0.020**	0.396	0.144	0.193	0.167
Hb (gm/dl)	-0.078	0.662	-0.506	**0.049**	-0.194	0.165
Serum Albumin (gm/l)	-0.285	0.102	0.144	0.608	-0.236	0.088
Corrected serum Ca (mmol/l)	-0.483	**0.004**	0.292	0.291	0.084	0.551
Serum PO_4 (mmol/l)	-0.037	0.834	0.017	0.953	0.705	**<0.001**
Serum iPTH (pg/ml)	0.721	**<0.001**	-0.259	0.351	0.682	**<0.001**

Table VI shows correlation of PASP in the study patients with different variables in different treatment groups. PASP had statistically significant positive correlation with age in all groups and duration of dialysis in those undergoing dialysis. PASP also positively correlated with serum creatinine but in only those not undergoing dialysis. PASP had statistically significant positive correlation with serum phosphate in HD group, serum iPTH in pre dialysis and HD groups and negatively correlated with corrected serum calcium in the pre dialysis group only. Serum hemoglobin negatively correlated with PASP in all patients but this was significant only in the CAPD group.

DISCUSSION

A total 102 patients were included in this study, out of which, 34 CKD stage 5 patients were in pre dialysis group, 53 patients were in the maintenance hemodialysis (HD) group and 15 patients were in the continuous ambulatory peritoneal dialysis (CAPD) group.

The present study demonstrated the frequency of pulmonary hypertension was 56.6% in HD, 13.3% in CAPD and 20.6% in pre dialysis patients. This is almost similar to Domenici et al. [17] who reported that pulmonary hypertension was found in 23/39 (58.9%) of the HD patients and 2/9 (22.2%) of the peritoneal dialysis patients.

Also Yigla et al. [5] reported that pulmonary hypertension was 39.7% in HD and in 1 of 8.33% in pre-dialysis patients. Abdelwhab and Elshinnawy demonstrated that pulmonary hypertension was 44.4% in HD and 32.3% in conservatively treated CKD patients [7]. In another study, Moniruzzaman et al. [18] found pulmonary hypertension 68.6% in HD and 8.6% in pre dialysis CKD patients.

Age was significantly higher in patients with pulmonary hypertension than without pulmonary hypertension. Similar finding was observed in the study of Emara et al. [19].

In this study, the effect of duration of dialysis in HD and CAPD treatment groups on pulmonary hypertension was seen. Mean duration of dialysis was significantly higher in patients with pulmonary hypertension than in non PH patients in both groups (HD and CAPD).

Mukhtar et al. [20] found a mean duration of HD in patients with pulmonary hypertension of 20.93 ± 12 months and for those without pulmonary hypertension the mean was 10.29 ± 10 months.

Among 37 patients with radial artery access, 20 (54.1%) had pulmonary hypertension and among 16 patients with brachial artery access, 10 (62.5%) had pulmonary hypertension. All of our patients had AVF. Emara et al. [19] reported that in those with a Brachial arteriovenous fistula (AVF) prevalence of pulmonary hypertension was 85.18% whereas among those with a radial AVF the prevalence was 14.81%.

In the pre dialysis group, there was a statistically significant higher serum creatinine and serum iPTH in pulmonary hypertension patients compared to those without pulmonary hypertension. There was a positive significant correlation of PASP with age, serum creatinine, and serum iPTH in this group and a negative significant correlation with corrected serum calcium. Emara et al. [19] found a significant positive correlation of PASP with serum creatinine and serum iPTH. They also found a negative correlation of PASP with corrected serum calcium similar.

As regards the peritoneal dialysis group, there was a significant positive correlation of PASP with age and duration of dialysis and a negative correlation of PASP with serum hemoglobin. Emara et al. [19] found a positive correlation of PASP with age and duration of dialysis but found no significant correlation of PASP with serum hemoglobin in their study.

Finally, in the HD group there was a positive significant correlation of PASP with age, duration of dialysis, serum phosphate, and serum iPTH in our study. Emara et al. [19] also found correlation of PASP

with age, duration of dialysis, serum phosphate and serum iPTH. Emara et al. [19] also found a significant positive correlation of PASP with serum creatinine.

CONCLUSION

This cross sectional study demonstrated a high frequency of pulmonary hypertension among patients with CKD on dialysis and pre dialysis. Pulmonary hypertension was found in 56.6% maintenance HD patients, in 13.3% CAPD patients and in 20.6% pre dialysis patients. Significant correlations of PASP with age, duration of dialysis, serum phosphate and serum iPTH were found. Early detection of pulmonary hypertension is important in order to avoid the serious consequences of the disease.

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