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Prevalence of Pulmonary Hypertension among Chronic Kidney Disease Patients and its Relation to Location and Blood Flow of Vascular Access

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Abstract

Background: Pulmonary hypertension is increasingly being recognized as a factor that can affect outcome in end stage renal disease. This study was carried out to evaluate the prevalence of pulmonary hypertension among CKD patients and it's relation to vascular access blood flow and location.

Patient and Methods: 30 patients on regular hemodialysis, 30 patients in predialysis and 30 healthy individuals participated in this study. Each patient underwent full clinical evaluation, chest radiography, pulmonary function tests, standard 12-lead electrocardiography, Two-dimensional and M-mode echocardiography. The fistulas were screened by Duplex ultrasound for evaluation of access flow. The 60 patients were divided according to pulmonary artery pressure (PAP) into patients with increased PAP (> 35 mmHg) and patients with normal PAP (< 35mmHg). Hemodialysis patients were divided according to location of fistula into brachial group and radial group.

Results: The means age were 52.2 ± 13 year, 55 ± 12 year and 55 ± 10 year for control group, CKD group and hemodialysis group respectively. Among hemodialysis patients 76.7 % had PHT, while 43.3% of CKD patients had PHT ($P < 0.005$). Patients with PHT had significantly longer duration of kidney disease, duration of hemodialysis and duration of AVF than those without PHT ($P < 0.001$). Patients with PHT had significant higher AVF blood flow ($P < 0.001$). 66.7%of patients with radial AVF had PHT, in contrast to all patients with brachial AVF had PHT ($p < 0.05$).

Conclusion: The prevalence of PHT is higher in patients receiving regular hemodialysis, and it is linked to shunt location and high AVF blood flow.

Keywords

CKD, Pulmonary hypertension, Shunt location, Access flow

Introduction

Pulmonary hypertension (PHT) is a progressive disorder complicating heart, lung, or systemic diseases, with increased morbidity and mortality regardless of its etiology [1]. In patients with end-stage renal disease (ESRD), PHT has been recognized to be a frequent condition and it appears to be independent from cardiovascular disease prevalence [2].

Metabolic and hormonal derangements caused by chronic renal failure may lead to pulmonary arterial vasoconstriction. Moreover, pulmonary calcification in chronic dialysis patients has been associated with pulmonary dysfunction. Besides, fluid overload and anemia may cause PHT. Since 1966, arteriovenous fistula (AVF), developed by Brescia and Cimino, has provided the best vascular access allowing long-term hemodialysis increased pulmonary artery pressure (PAP) was found in chronic renal failure patients with surgically created AVF [3].

Although there are probably genetic determinants, environmental exposures and acquired disorders that predispose the patients to PHT, it is clear that none of the factors alone is sufficient to activate the pathways essential for the development of this vascular disease [4,5]. After creation of AVF, many patients experience an instantaneous decrease in peripheral vascular resistance that results in a compensatory increased cardiac output [6]. Cardiac stress of the AVF causes a variety of changes including diastolic dysfunction, congestive heart failure, PHT, and, finally cardiomyopathy [6-8]. The aim of this study is to evaluate the prevalence of pulmonary hypertension among CKD patients and it's relation to the shunt location and AVF blood flow.

Materials and Methods

The study was performed in Al-Hussein University Hospital from December 2013 to Jun 2014. Sixty patients (32 male and 28 female) involved in this study of different age group ranging from (30 to 80) years (mean of age 54.7 ± 12 year) complaining chronic renal failure. 30 patients on regular hemodialysis (hemodialysis group) and 30 patients in predialysis (CKD group), glomerular filtration rate (GFR) assessed by Cockrauft and Gault formula [9]. Thirty healthy individuals (16 male and 16 female) were used as control group. None of the participants suffered from chronic obstructive lung disease; interstitial lung disease; chest wall disease; primary pulmonary hypertension; previous pulmonary embolism; collagen vascular

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Table 1: Comparison between studied groups

Parameters	Control	CKD	HD patients	P
No. of patients	30	30	30	
Age (years)	52.2 ± 13	55 ± 12	56 ± 10	> 0.05
Sex Male: (n, %) (46, 51.1%) Female: (n, %) (44, 48.9%)	 14, 15.6 % 16, 17.8%	 18, 20% 12, 13.3%	 14, 15.6 % 16, 17.8%	 > 0.05
Body mass index	29.1 ± 6.6	27.1 ± 6.2	27.9 ± 5.9	> 0.05
Systolic blood pressure (mmHg)	129 ± 8	136 ± 20	135 ± 14	> 0.05
Diastolic blood pressure (mmHg)	83 ± 4.3	83 ± 8	83 ± 7	> 0.05
Heart rate (b /min)	93 ± 8	85 ± 8.6	90 ± 9	< 0.001
Serum creatinine (mg/dl)	0.74 ± 0.12	3.9 ± 0.9	8.1 ± 1.9	< 0.001
Blood urea(mg/dl)	27.5 ± 10	110 ± 44	155 ± 35	< 0.001
eGFR (ml/min)	107 ± 8.9	24.8 ± 5.9	------	< 0.001
Serum calcium (mg/dl)	9.8 ± 0.57	8.6 ± 0.88	8.6 ± 0.75	> 0.05
Serum phosphorus (mg/dl	4.5 ± 0.32	5.4 ± 0.95	6.0 ± 1.1	< 0.001
Parathyroid hormone (pg/ml)	28 ± 14	227 ± 103	449 ± 259	< 0.001
Hemoglobin levels (g/dl)	12.2 ± 1.1	10.8 ± 1	10.8 ± 1.3	< 0.001
Serum uric acid (mg/dl)	6.5 ± 1.5	7.1 ± 1.6	6.2 ± 1.24	> 0.05
Serum albumin (g/dl0	4.2 ± 0.32	3.5 ± 0.63	3.8 ± 0.47	< 0.001
Random blood glucose (mg/dl)	106 ± 17	116 ± 20	115 ± 21	> 0.05
Cholesterol (mg/dl0	200 ± 17	211 ± 20	212 ± 27	> 0.001
Triglycerides (mg/dl)	144 ± 26	142 ± 34	154 ± 47	> 0.001
LDL (mg/dl)	106 ± 9.6	109 ± 15.6	114 ± 16.7	> 0.001
Left ventricular end diastolic dimension (mm)	4.62 ± 0.45	5.18 ± 0.96	5.16 ± 0.81	< 0.05
Left ventricular end systolic dimension (mm)	3.07 ± 0.47	3.53 ± 0.89	3.83 ± 0.87	< 0.05
Ejection fraction %	68.9 ± 4.6	65.3 ± 4.5	64.2 ± 7.4	< 0.05
Fractional shortening %	37.8 ± 2.4	36 ± 2.6	35.5 ± 4.2	< 0.05
Left atrial dimension (mm)	3.2100	4.1333	4.2633	< 0.001
cardiac output (ml/min)	5908 ± 296	6494 ± 1026	7921 ± 655	< 0.001
Pulmonary artery pressure (mmHg)	23 ± 3.8	36 ± 9	44 ± 10	< 0.001

Table 2: Clinical data of patients with PHT and patients without PHT

Parameters	Patients without PHT	Patients with PHT	P
Number of patients	24 (40%)	36 (60%)	
Age (years)	52.6 ± 12	58 ± 10	> 0.05
Sex (n,%) Male: 32 (53.3%) Female: 28 (46.7%)	 13 (21.7%) 11 (18.3%)	 19 (31.7 %) 17 (28.3%)	 > 0.05
Etiology of renal disease: (n, %) Diabetic nephropathy 20(33.3%) HTN 15 (25%) Glomerulonephritis 7 (11.7%) Obstructive uropathy 5 (8.3%) ADPKD 2 (3.3%) Ch. Pyelonephritis 5 (8.3%) Undetermined renal 6 (10%)	 5 (25%) 5 (33.3%) 4 (57.1%) 2 1 2 6	 15 (75%) 10 (66.7%) 3 (42.9%) 3 1 3	 > 0.05
Antihypertensives (n, %)	16 (34.8%)	30 (65.2%)	
Ca channel blockers	7(15.8%)	14(30.4%)	> 0.05
Beta blockers	3(6.5%)	1(2.2%)	
ACE inhibitors	6(13%)	15(32.6%)	
Antidiabetics (n, %)			
Insulin	5(25%)	15(75%)	
Valdagliptin	3(15%)	8(40%)	
No treatment	2(10%)	4(20%)	> 0.05
Hemodialysis (n, %)	0	3(15%)	
Predialysis CKD patients	17(56.7%)	13(43.3%)	< 0.005
Hemodialysis patients	7(23.3%)	23(76.7%)	
Shunt location (n %)			
Brachial	00	9(100%)	< 0.05
Radial	7(33.3%)	14(66.7%)	

disease; left to right shunt and moderate or severe mitral or aortic valve disease. Also, we excluded patients dialyzed via catheters and those with volume overload at the time of echocardiography. Each patient underwent full clinical evaluation with special emphasis on any clinical condition that predisposes to pulmonary hypertension, chest radiography, and pulmonary function tests (PFTs), standard 12-lead electrocardiography (ECG) before enrollment to the study. The sixty patients were divided according to PAP into patients with increased PAP (> 35mmHg) and patients with normal PAP (< 35mmHg). In addition, hemodialysis patients were divided according to location of their fistula into brachial group and radial group.

The fistulas were screened by Duplex ultrasound from the brachial artery in the mid arm via anastomosis and upward to the upper arm. The flow measurement of the feeding artery (supplier proximal artery to the shunt) was taken 2cm. above the fistula. For the evaluation of access flow, the diameter and cross sectional area of the feeding artery were determined by a B-mode sonography in a transverse plane from the inner edge to the inner edge and tracing the luminal outline. At the same site, Doppler spectra were obtained in a longitudinal plane with an angle maintained as far as possible at ≤ 60° (45°–65°) for calculation of time averaged velocity (TAV). Access flow was determined by equipment software using the formula below: Flow volume (mL/min) = TAV (cm/sec) × πr^2 (cross -sectional area in cm^2) × 60 [9]. To reduce errors to an acceptable level, we carried out the measurements twice and used the mean results. If the second measurement varied by > 10%, then a third measurement was performed and the mean of the two closest measurements were recorded. The studies were performed by one radiologist who was not aware of the clinical, laboratory or hemodialysis status when performing the ultrasound examination.

Two-dimensional and M-mode echocardiography was performed. A tricuspid systolic jet was recorded from the parasternal or apical window with the continuous-wave Doppler probe. The pulmonary artery systolic pressure (PASP) or systolic right ventricular pressure was calculated using the Bernoulli equation: PASP = 4 × (tricuspid systolic jet) 2 + 10mmHg (estimated right atrial pressure) [10]. Pulmonary hypertension was defined as a PASP ≥ 35mmHg [11]. All patients were informed about the content of the study and gave their written approvals before enrollment. All procedures were performed in accordance with the ethical standards of Al-Azhar University's committee on human experiments.

Statistical analysis

All statistical analysis was performed using the SPSS 17.0 software. Values were expressed as mean ± Standard deviation (SD) and as percentage for categorical parameters. One-way analysis of variance (ANOVA) was used for comparison between multiple groups. Student -t was used for comparison between two independent groups. Chi-square test was applied for estimating the occurrence of categorical variables. Pearson's correlation coefficient was used to test the relationship between PAP and other variables.

Results

Characteristics of the 90 participants investigated are summarized in the table 1, table 2, table 3 and table 4. The means of their age were 52.2 ± 13 year, 55 ± 12 year and 55 ± 10 year for control group, CKD group and hemodialysis group respectively. The common etiologies of renal failure were diabetes (33.3%), hypertension (25%) and glomerulonephritis was (11.7%) (Table 2). Among hemodialysis patients 76.7 % had PHT, while 43.3% of CKD patients had PHT (P < 0.005). The means PAP were (42 ± 15mmHg, 28.9 ± 12mmHg, 20 ± 2.4mmHg) for hemodialysis patients, predialysis patients and normal subjects respectively (P < 0.001) (Table 1). As regards to echocardiographic parameters we found also statistical differences in cardiac output (CO), and left atrial dimension (LA) (p < 0.001), left

Table 3: Comparison between with PHT and without PHT as regards to aboratory parameters.

Parameters	Patients without PHT	Patients with PHT	P
Duration of CKD (months)	18.13 ± 7	57.7 ± 41	< 0.001
Duration of hemodialysis (months)	19.8 ± 8	60 ± 40	< 0.001
Duration of AVF (months)	23 ± 14	57.4 ± 40	< 0.001
Body mass index	28.8 ± 6.2	26.4 ± 4.9	> 0.05
Systolic blood pressure (mmHg)	133 ± 18	137 ± 16	> 0.05
Diastolic blood pressure (mmHg0	82 ± 7	84 ± 7	> 0.05
Heart rate (beat /min)	84 ± 6.8	90 ± 9.8	< 0.05
Serum creatinine (mg/dl)	5.2 ± 2.6	6.6 ± 2.4	> 0.001
Blood urea (mg/dl)	120 ± 38	140 ± 48	> 0.001
eGFR (ml/min)	26 ± 5.4	22.9 ± 4.8	> 0.05
KT/V	1.45 ± 0.13	1.44 ± 0.18	> 0.05
Serum calcium (mg/dl)	8.7 ± 1	8.6 ± 0.67	> 0.05
Serum phosphorus (mg/dl)	5.30 ± 1.1	6.0 ± 0.9	< 0.005
Parathyroid hormone (pg/ml)	270 ± 226	384 ± 216	> 0.05
Hemoglobin levels (g/dl)	11.4 ± 1	10.4 ± 1.1	< 0.005
Serum uric acid (mg/dl)	6.7 ± 1.4	6.6 ± 1.7	> 0.05
Serum albumin (g/dl)	3.8 ± 0.6	3.8 ± 0.7	> 0.05
Random blood glucose (mg/dl)	115 ± 15	116 ± 23	> 0.05
Cholesterol (mg/dl)	219 ± 23	207 ± 23	> 0.05
Triglycerides (mg/dl)	150 ± 29	147 ± 48	> 0.05
LDL (mg/dl)	111 ± 14	112 ± 17	> 0.05
Left ventricular end diastolic dimension (mm)	4.60 ± 0.4	5.55 ± 0.8	< 0.001
Left ventricular end systolic dimension (mm)	3.0 ± 0.4	4.13 ± 0.8	< 0.001
Ejection fraction %	67.2 ± 4.1	63.1 ± 6.7	< 0.05
Fractional shortening %	37.16 ± 2.4	34.88 ± 3.8	< 0.05
Left atrial dimension (mm)	3.73 ± 0.53	4.50 ± 0.65	< 0.001
cardiac output (ml/min)	6607 ± 1031	7607 ± 996	< 0.001
Pulmonary artery pressure(mmHg)	30 ± 3	47 ± 8	< 0.001
AVF blood flow (ml/min)	840.7 ± 154	1228 ± 238	< 0.001

Table 4: Comparison between patients as regards to location of shunt.

	Bronchial AVF	Radial AVF	P
Age (years)	58 ± 14	55 ± 9	> 0.05
Duration of CKD (months)	114 ± 22	39.5 ± 29	< 0.001
Duration of hemodialysis (months)	97.7 ± 26	30.6 ± 24	< 0.001
Duration of AVF(months)	93.8 ± 28	30.3 ± 24	< 0.001
Body mass index	28.2 ± 5.7	27.4 ± 4.7	> 0.5
Systolic blood pressure (mmHg)	136 ± 10	134 ± 15	> 0.5
Diastolic blood pressure (mmHg)	86 ± 7	82 ± 7	> 0.5
Heart rate (beat /min)	95 ± 10	88 ± 7	> 0.5
Serum creatinine (mg/dl)	8.9 ± 1.8	7.75 ± 1.9	> 0.5
Blood urea (mg/dl)	153 ± 35	153.8 ± 36	> 0.5
KT/V	1.3 ± 0.19	1.4 ± 0.16	> 0.5
Serum calcium (mg/dl)	8.9 ± 0.6	8.5 ± 0.7	> 0.5
Serum phosphorus (mg/dl)	6.5 ± 0.7	5.9 ± 1.2	> 0.5
Parathyroid hormone (pg/ml)	477 ± 302	437 ± 246	> 0.5
Hemoglobin levels (g/dl)	9.9 ± 1.4	11 ± 1.2	< 0.05
Serum uric acid (mg/dl)	6.1 ± 0.6	6.4 ± 1.7	> 0.5
Serum albumin (g/dl)	4.1 ± 0.4	4.1 ± 0.6	> 0.5
Random blood glucose (mg/dl)	118 ± 41	114 ± 59	> 0.5
Cholesterol (mg/dl)	198 ± 18	219 ± 28	> 0.5
Triglycerides (mg/dl)	143 ± 52	159 ± 43	> 0.5
LDL (mg/dl)	111 ± 17	116 ± 16	> 0.5
Left ventricular end diastolic dimension (mm)	5.2 ± 0.7	5.1 ± 0.8	> 0.5
Left ventricular end systolic dimension (mm)	4.2 ± 0.6	3.6 ± 0.9	> 0.5
Ejection fraction %	59.5 ± 9	66 ± 5.8	> 0.5
Fractional shortening %	32.8 ± 5	36.6 ± 3.2	> 0.5
Left atrial dimension (mm)	4.7 ± 0.4	4 ± 0.8	< 0.05
cardiac output (ml/min)	8305 ± 437	7757 ± 672	< 0.05
Pulmonary artery pressure(mmHg)	53.6 ± 9.7	37 ± 14	< 0.005
AVF blood flow (ml/min)	1397 ± 163	1027 ± 237	< 0.001

ventricular end diastolic dimension (LVEDD), left ventricular end systolic dimension (LVESD), ejection fraction (EF%), and fractional shortening (FS)(P < 0.05) between studied group (Table 1).

Table 5: Correlation between pulmonary artery pressure and other parameters

	ePAPs mmHg	
	r	Sig
Age (years)	.341**	0.001
Duration of CKD (months)	.686**	0.000
Duration of hemodialysis (months)	.667**	0.000
Duration of AVF(months)	.610**	0.000
BMI	-.196	0.065
Systolic BP/mmHg	.163	0.126
Diastolic BP/mmHg	.126	0.236
Heart Rate(beat /min)	-.065	0.543
Serum Creatinine (mg/dl)	.719**	0.000
Blood Urea (mg/dl)	.620**	0.000
Serum calcium (mg/dl)	-.179	0.343
Serum phosphorus (mg/dl)	.649**	0.000
PTH (pg/ml)	635**	0.000
Hemoglobin (g/dl)	-.609**	0.000
Serum Uric acid (mg/dl)	.101	0.343
Serum Albumin (g/dl)	.132	0.214
Fasting blood Glucose (mg/dl)	.154	0.148
Serum Cholesterol (mg/dl)	-.128	0.230
Serum Triglycerides (mg/dl)	-.106	0.320
LDL (mg/dl)	.136	0.202
A-V fistula flow (ml/min)	.742	0.000

**Correlation is significant at the 0.01 level.

*Correlation is significant at the 0.05 level.

Among 60 patients we found 36 patients (60%) had PHT, mean age was 58 ± 10 years, 19 patients (31.7%) were males and 17 patients (28.3%) were females. In addition to, 24 patients (40%) without PHT, mean age was 52.6 ± 12 years, 13 patients (21.7%) were males and 11 patients(18.3%) were females. 75% of diabetic patients had PHT, also 66.7% of hypertensive patients had PHT. Patients with PHT had significantly longer duration of kidney disease, duration of hemodialysis and duration of functioning AVF than those without PHT (P < 0.001). Moreover, patients with PHT had significant higher AVF blood flow, cardiac output, left atrium dimension, left ventricular end diastolic dimension, left ventricular end systolic dimension (P < 0.001),ejection fraction and fractional shortening (P < 0.05) than those without (Table 2,3).

Among hemodialysis patients, there are 14 out of 21 patients (66.7%) with radial AVF location had PHT, in contrast to 9 patients (100%) with brachial AVF location had PHT (p < 0.05) (Table 2). Comparison between patients with brachial AVF with those with radial AVF revealed that patients with brachial AVF location had significant longer duration of renal disease, duration of hemodialysis and duration of AVF(P < 0.001), also they had lower hemoglobin levels (p < 0.05) and higher AVF blood flow (P < 0.001). Moreover, the patients with brachial AVF location had higher cardiac output, left atrial dimension (P < 0.05) and pulmonary artery pressure (P < 005) (Table 4).

As shown in table 5, pulmonary artery pressure is significant positive correlated with age, duration of hemodialysis, duration of AVF, serum creatinine, blood urea, PTH, and AVF fistula blood flow (P < 0.001). and negative correlated with hemoglobin and serum uric acid(P < 0.001).

Discussion

The results of the present study indicate a very high prevalence of PHT (60 %) among CKD and it was higher among hemodialysis patients (76.7%). Published literature reported prevalence of PHT was ranges from 9-39% in predialysis patients [12-15], 18.8-68.8% in hemodialysis patients, and 0-42% in individuals on peritoneal dialysis therapy [16-23]. The variation in prevalence may be due to the timing of performance of echocardiograms, as it may influence prevalence estimates. Varying definitions of pulmonary hypertension may account for varying prevalence estimates. Method of PAP measurement "by echocardiography assessment or by central venous

catheterization". As well as, variable degrees of chronic volume overload may confound the prevalence. Since there are no agreed upon markers for chronic volume overload, it is difficult to account for this variable among studies.

We observed no differences between hemodialysis patients and pre-dialysis CKD patients according to age, sex, body mass index (BMI), systolic and diastolic blood pressure, serum calcium, serum uric acid, blood sugar, cholesterol, triglycerides and LDL. Tarrass et al. [24] demonstrated that no significant differences between both groups with regards to age, sex, duration of dialysis, shunt location, and all the biological parameters of the study. The presence of PH was not related to the level of PTH, or the severity of other metabolic abnormalities. Similar results achieved by Fabbian et al. [21] demonstrated that age, calcium, phosphate, PTH concentrations and history of parathyroidectomy revealed no difference between those with and without PHT. Our hemodialysis patients had significant higher The Doppler-estimated pulmonary artery systolic pressure (ePAPs) than pre-dialysis CKD patients. Also, they had significantly higher heart rate, serum creatinine, blood urea, serum phosphorus, parathyroid hormone (PTH) and cardiac output than pre-dialysis patients. Moreover, ePAPs was significantly direct correlated to age, duration of kidney disease, duration of hemodialysis, duration of AVF, serum creatinine, blood urea, serum phosphorus, PTH and AVF blood flow and indirect significant with hemoglobin. These results in concordance with, Havlucu et al. [13] found that chronic renal failure duration was positively correlated with PAP. Also, Manuti [25] demonstrated that the presence of pulmonary hypertension was related to presence of arteriovenous fistula and long duration of hemodialysis. Abdallah et al. [26] demonstrated that CKD duration and AV fistula duration were positively correlated with systolic PAP in patients receiving hemodialysis. Also, Fabbian et al. [21], Emara et al. [27] demonstrated that the group of subjects with PHT had higher dialysis vintage. In contrast, Amin et al. [28] and Tarrass et al. [24] reported that there was no significant difference between patients with PHT and those without PHT as regards to duration of dialysis. *Yang* and *Bao* [29] demonstrated that renal functions were negatively correlated with PAPs. Buemi et al. [12] demonstrated association between PHT and anemia. Factors associated to PHT in subjects treated with HD and pre dialysis CKD seems to be different, probably reflecting a different degree of chronic volume overload, exposure to dialysis membranes, effect of AVF blood flow, inflammatory mediators, these factors are responsible to some extent for PHT.

Gender has also been implicated as an independent risk factor for PHT. Various studies have demonstrated that PHT is detected more frequently in women than in men. Amin et al. [28] reported a higher prevalence of PHT, 48% in women. Havlucu et al. [13] reported that, female to male ratio of patients with PHT was 60% vs. 40%. Mukhtar et al. [30] also found higher prevalence in females, 52% compared to 48% in males that was statistically significant. Our study found prevalence in females, 28.3% compared to 31.7% in males that was statistically non-significant. Similarly, various studies could not find association between gender and development of PHT Kumbar et al. [16], Fabbian et al. [21] and Tarrass et al. [24] found no difference between male and female.

In the present study we found significant higher levels of serum creatinine, blood urea, serum phosphorus, and significant low hemoglobin levels in patients with PHT than those without PHT. This results demonstrated by Nakhoul et al. [6], decreased eGFR and hemoglobin level may increase pulmonary artery pressure due to volume overload and increased pulmonary blood flow due to anemia. Yigla et al. [3] compared data on 23 patients with PHT receiving hemodialysis with 35 patients without PHT receiving hemodialysis. They demonstrated that, the hemoglobin and hematocrit levels were significantly lower in the PHT subgroup. Magdy et al. [27] demonstrated that higher serum creatinine, and phosphorous levels, lower hemoglobin and hematocrit in patient with PHT than those without. But no differences were found between groups with respect to age and PTH. On the other hand, Amin et al. [28] reported that there was no difference between patients with PHT and those without PHT as regards to serum calcium, phosphorus, alkaline phosphatase and PTH.

In the present study, significant increase in PAPs, LVEDD, LVESD, left atrium size and COP were detected in patients with PHT associated with decrease in EF and FS. These results in concordance with Yigla et al. [3], Havlucu et al. [13] and Abdallah et al. [26] they found that the cardiac output was significantly higher among the PHT subgroup of CKD. Beigi et al. [31], Fabbian et al. [21], Emara et al. [27] and Mehdi et al. [32], reported an inverse correlation between PAP and ejection fraction. The increase in left atrium size, COP, LVEDD and LVESD and the decrease in EF% and FS% may reflect chronic volume overload, effect of AVF on the heart or poor myocardial performance [22].

In clinical practice, shunting of blood from the left to the right side of the heart and increased cardiac output and pulmonary blood flow are common medical conditions resulting in PHT [31]. Our results demonstrated that, a highly significant increase in AVF blood flow in patients with PHT compared to patients with normal pulmonary artery pressure. In addition, there was positive significant correlation between PAP and AVF blood flow. Nakhoul et al. [6] reported that PAP increased significantly following initiation of hemodialysis therapy via A-V access and decreased significantly after successful kidney transplantation, as well as after short A-V access compression, indicating that both ESRD and A-V access contribute to the pathogenesis of PHT. Also, Clarkson et al. [33] reported PHT of 60mmHg in an ESRD patient receiving chronic HD therapy via an aneurysmal brachicephalic A-V fistula. In line with our finding, surgical ligation of the A-V fistula and insertion of a tunnelled semi-permanent internal jugular dialysis catheter reduced the PAP to 30mmHg. Havlucu et al. [13], Abdelwhab and Elshinnawy [14], Abdallah et al. [26], Beigi et al. [31], and Mehdi et al. [32] demonstrated that hemodialysis patients with PHT have a significantly higher AVF blood flow and PAP correlates with AVF flow.

Because the study population had no obvious cause for PHT, they assumed that some factors, such as the size or the location of arteriovenous fistulae are involved in the mechanism that increases cardiac output and contribute to the pathogenesis of pulmonary hypertension. In this study, 9 patients (100%) with brachial AVF had PHT in comparing to 14 patients out of 21 patients (66.7%) with radial AVF had PHT. Comparing data of patients with brachial AVF and patients with radial AVF, there were significantly high age, ePAPs, COP and AVF blood flow in patients with brachial AVF. Mehdi et al. [32] reported that, obvious higher fistula flow rate in patients with PHT, and main determinants of fistula flow are location of the fistula and artery diameter. On the other hand, Tarrass et al. [24] demonstrated that, the effect of AVF location was not statistically significant.

Lower arm AVFs are usually positioned in a type of patient with a different phenotype from those who get an upper arm AVFs (among them, usually there are less diabetics, younger people with fewer vascular diseases and cardiac dysfunctions). Depends on our data, fistula that is created in a large vessels has higher AVF blood flow, higher COP, increased sympathetic activity resulting in an increase in myocardial contractility and heart rate, increased pulmonary blood flow. All these factors may induce pathophysiological response upon the three components of pulmonary artery pressure that include volume of pulmonary blood flow, resistance in the pulmonary vascular bed and pulmonary venous pressure. Magdy et al. [27] demonstrated that patients with PHT had higher AV fistula flow, 85% of patients with brachial AVF had PHT, in contrast to 40 % of patients with radial AVF 23 had PHT.

Conclusion

This study demonstrated that 76.7% of patients with ESRD receiving regular hemodialysis have PHT. Findings support a role of shunt location and high AVF blood flow as the etiology of PHT in these patients.

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