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Original research article

STUDY TO EVALUATE THE PREVALENCE OF PULMONARY ARTERIAL HYPERTENSION AND ITS RISK FACTORS ASSOCIATED WITH THE DEVELOPMENT IN INDIVIDUALS WITH CHRONIC RENAL DISEASE

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Abstract

Aim: To evaluate the prevalence of pulmonary arterial hypertension in individuals with chronic renal disease and to investigate the risk factors associated with the development of this condition in these patients.

Methods: This was an observational cross section study conducted on 100 patients of CKD (based on KDIGO 2012 criteria) attending hospital OPD.

Results: Pulmonary hypertension was detected in 60 individuals (60%) within the research cohort. The occurrence of pulmonary hypertension was not significantly associated with age, BMI, prevalence of diabetes, or serum uric acid levels. A strong correlation was seen between systolic and diastolic blood pressure and PH. There was a significant correlation between the severity of chronic kidney disease (CKD) and pulmonary hypertension (PH). The presence of hemodialysis and the length of dialysis were strongly correlated with the occurrence of pulmonary hypertension (PH). Out of a total of 60 patients diagnosed with pulmonary hypertension (PH), 23 patients had mild PH, 32 patients had moderate PH, and 5 patients had severe PH.

Conclusion: Our findings indicate a substantial association between pulmonary arterial hypertension (PAH) and chronic kidney disease (CKD). Furthermore, we observed that the severity of PAH increases as renal function deteriorates in CKD patients. Risk factors for the development of pulmonary arterial hypertension (PAH) include anaemia, prolonged dialysis duration, hypertension, hyperparathyroidism, AV fistula, elevated calcium phosphate product, and left ventricular failure.

Keywords: Pulmonary arterial hypertension, chronic kidney disease, risk factors

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Introduction

Pulmonary hypertension (PH) is characterized by a mean pulmonary arterial pressure (PAP) of 425 mm Hg, as determined during right heart catheterization. Pulmonary hypertension (PH) may emerge as a secondary condition due to an underlying cardiac or pulmonary issue, or it can develop independently when there is a primary pulmonary arteriopathy. Irrespective of the cause, a long-lasting increase in pulmonary artery pressure (PAP) results in impaired functioning of the right ventricle, leading to associated illness and death [1-7]. PH has lately been acknowledged as a prevalent consequence of chronic kidney disease (CKD) and end-stage renal disease (ESRD). In order to comprehend this connection, it is crucial to examine the hemodynamic factors that contribute to pulmonary hypertension (PH) and to define the range of illnesses that might lead to PH.

In routine medical practice, pulmonary arterial pressure (PAP) is assessed using echocardiography by employing the modified Bernoulli equation: PAP = 4 X (velocity of the tricuspid systolic jet)2 + estimated right atrial pressure. The latter is usually determined by measuring the diameter of the vena cava or by assigning a predetermined, constant value [8, 9]. The limits of echocardiography in definitively identifying pulmonary hypertension (PH) are well recognised. These limitations include mistakes in measuring pulmonary pressure when the tricuspid jet is limited or difficult to perceive, as well as the dependence on indirect or assumed measures of right atrial pressure [10].

However, the regular use of echocardiography to indirectly determine pulmonary hypertension (PH) is influenced by several factors, such as cost-effectiveness, the safety of noninvasive measurements, the convenience of using it as a screening tool, and the greater accessibility of echocardiography compared to right heart catheterization. The significance of right cardiac catheterization in examining pulmonary hypertension (PH) in patients with renal illness cannot be overstated, notwithstanding the aforementioned benefits. Pulmonary hypertension (PH) in end-stage renal disease (ESRD) or chronic kidney disease (CKD) is a complex condition influenced by several factors. Echocardiography has limitations in accurately determining the specific impact of cardiac output (CO), pulmonary capillary wedge pressure (PCWP) and pulmonary vascular resistance (PVR) on the high pulmonary artery pressure (PAP) [11]. Pulmonary hypertension (PH) is mainly a condition affecting the tiny arteries of the pulmonary vasculature. It involves the gradual narrowing of these arteries, resulting in higher pulmonary vascular resistance (PVR) and pulmonary arterial pressure (PAP), which are defining features of the illness [12]. Elevated pulmonary vascular resistance (PVR) often results in right ventricular failure, which is linked to a high death rate [13].

The objective of this research was to evaluate the prevalence of pulmonary arterial hypertension in individuals with chronic renal disease and to investigate the risk factors associated with the development of this condition in these patients.

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Materials and Methods

This was an observational cross section study conducted on 100 patients of CKD (based on KDIGO 2012 criteria) attending hospital OPD.

Inclusion criteria

1. Patients of CKD in stage IV and stage V.
2. Age ≥18 years.

Exclusion criteria

- Valvular heart disease.
- Congenital heart diseases.
- Chronic obstructive pulmonary disease.
- Chronic parenchymal lung disease.
- HIV-infected patients.
- Chronic liver disease.
- Connective tissue diseases.
- Hypothyroidism and hyperthyroidism.
- Pregnancy.
- Chronic thromboembolic disorders.

Methodology

Each patient was subjected to detailed history and clinical examination and relevant investigations were done including CBC, KFT, random blood sugar, S. Electrolytes, S. Calcium, S. Phosphate, S. iPTH, S. uric acid, urine routine and microscopy, USG abdomen, Chest X-Ray, ECG and echocardiography. PAH was diagnosed on the basis of echocardiography with mean pulmonary arterial pressure (MPAP) of ≥25mmHg at rest was taken as diagnostic of pulmonary arterial hypertension.

Pulmonary hypertension was classified as:

- Mild (25-40 mHg).
- Moderate (40-60 mmHg).
- Severe (>60 mmHg).

Statistical analysis

Quantitative variables were compared using unpaired t-test/Mann- Whitney Test (when the data sets were not normally distributed) between CKD. Qualitative variables were compared using Chi-Square test/Fisher's exact test. A p value of <0.05 was considered statistically significant. The data was entered in MS EXCEL spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0.

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Results

Table 1: Characteristics of patients with mild, moderate and severe PH

Parameters	Mild PH (n=23)	Moderate PH (n=32)	Severe PH (n=5)	P value
Age	33.57 ± 10	30 ± 6.44	42.48 ± 2.08	0.001
BMI	23.47 ± 1.52	24.48 ± 1.36	23.57 ± 3.14	0.010
SBP	144.06 ± 12.28	148.32 ± 8.52	146.4 ± 20.32	0.004
DBP	85.75 ± 7.03	86.34 ± 7.3	88 ± 8.56	0.232
CKD stage 4	16	4	0	<0.0001
CKD stage 5	6	28	5	<0.0001
Presence of Hemodialysis	12	27	5	0.068
Hemodialysis duration (weeks)	6.44 ± 1.74	13.47 ± 5.35	18.2 ± 1.88	<0.0001
Presence of AVF	0	14	6	0.001
Presence of Diabetes	6	2	4	0.0003
Hemoglobin	7.53 ± 0.32	7.24 ± 0.52	6.84 ± 0.3	<0.0001
S. Uric Acid	7.12 ± 1.02	6.74 ± 0.89	8.22 ± 0.62	0.071
S. Calcium	7.8 ± 0.52	7.30 ± 0.38	7.35 ± 0.72	0.077
S. Phosphate	6.84 ± 0.54	7.03 ± 0.2	7.18 ± 0.12	<0.0001
Calcium Phosphate Product	49.31 ± 3.4	51.59 ± 2.87	54.46 ± 4.20	<0.0001
iPTH	348.62 ± 54.46	426.74 ± 44.76	459.5 ± 9.31	<0.0001
LVEF%	38.32 ± 4.26	34.56 ± 6.04	36 ± 7.07	0.001

Of 60 PH patients, 23 had mild, 32 moderate, and 5 (8.34%) severe. High systolic blood pressure substantially enhanced PH severity. PH severity increased with CKD stage. PH severity increased with dialysis time and AVF. Lower hemoglobin, higher serum phosphate, calcium phosphate product and intact parathormone were also linked to PH severity. PH severity increased with low LVEF%.

Table 2: Multivariate logistic regression to find out independent significant risk factor of pulmonary hypertension

	Beta coefficient	Standard P value	Lower bound (95%)	Upper bound (95%)
Systolic blood pressure (mmHg)	-0.024	0.053	0.840	1.080
Diastolic blood pressure (mmHg)	0.044	0.100	0.890	1.276
Dialysis duration (weeks)	-0.185	0.206	0.590	1.260
Haemoglobin (gm/dL)	-1.150	1.585	0.018	7.376
S. Calcium (mg/dL)	-14.270	9.752	0.000	124.350
S. Phosphate (mg/dL)	-15.368	10.786	0.000	266.712
Calcium Phosphate product	2.120	1.432	0.525	131.787
Intact parathormone (pg/mL)	0.009	0.014	0.981	1.032
LVEF%	-0.043	0.093	0.798	1.149

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CKD stage				
5	1.555	1.936	0.083	219.139

On performing multivariate logistic regression after adjusting for confounding factors, none of the factors was found to be an independent significant risk factor for pulmonary hypertension.

Discussion

Chronic kidney disease (CKD) is primarily associated with cardiovascular disease, which is the leading cause of illness and death in these people [14]. The primary emphasis is often placed on the adverse impact of left ventricular failure, which leads to higher rates of illness and death in patients with chronic kidney disease (CKD). However, pulmonary arterial hypertension (PAH), a cardiovascular consequence of CKD, particularly in end-stage renal disease (ESRD), is often disregarded. Increased pulmonary arterial pressure (PAP) may be noticed as a result of heart, lung, or systemic problems. Pulmonary arterial hypertension (PAH) is characterized by a resting mean pulmonary artery pressure of 25 mmHg or higher, or a mean pulmonary artery pressure of 30 mmHg or higher during activity [15]. Navaneethan *et al*. observed a higher death rate in a group of patients with pulmonary hypertension (PH) and chronic kidney disease (CKD). However, they did not examine a community of CKD patients specifically to determine the occurrence of PH. The hemodynamic characteristics of pulmonary hypertension (PH) in individuals with chronic kidney disease (CKD) have not been well investigated, particularly in distinguishing between pre-capillary PH and post-capillary PH. Consequently, it is necessary to conduct research that use invasive hemodynamics to understand the cause of pulmonary hypertension (PH) in patients with chronic kidney disease (CKD). Furthermore, previous research has been deficient in providing details on significant co-morbidities and echo factors that might potentially impact the association between pulmonary hypertension (PH) and chronic kidney disease (CKD).

Pulmonary hypertension was detected in 60 individuals (60%) within the research cohort. The presence of pulmonary hypertension was not significantly associated with age, BMI, diabetes, or serum uric acid levels. A significant correlation was seen between systolic and diastolic blood pressure and PH. A significant correlation was seen between the severity of chronic kidney disease (CKD) and pulmonary hypertension (PH). The presence of hemodialysis and the length of dialysis were strongly correlated with the occurrence of pulmonary hypertension (PH). A strong correlation was seen between the existence of arteriovenous fistula (AVF) and the occurrence of pulmonary hypertension (PH). The presence of low haemoglobin was shown to have a strong correlation with pulmonary hypertension (PH). The presence of PH was substantially related with low blood calcium, high serum phosphate, elevated calcium phosphate product, and higher intact parathormone levels. Patients diagnosed with pulmonary hypertension had a decreased left ventricular ejection fraction percentage. Zhang *et al*. [17] found similar outcomes, with individuals with greater BMI experiencing more severe PH. Nevertheless, research conducted by K. Ramasubbu *et al*. [18] revealed that individuals with more severe pulmonary hypertension had a decreased body mass index (BMI). Obesity is a known risk factor for the development

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of cardiovascular disease, diabetes mellitus, hypertension, renal disease, and metabolic abnormalities. However, the relationship between body mass index (BMI) and the severity of pulmonary hypertension (PH) is not clear, since the findings of studies investigating this correlation have been inconsistent.

Out of a total of 60 patients diagnosed with pulmonary hypertension (PH), 23 patients had mild PH, 32 patients had moderate PH, and 5 patients had severe PH. There was a significant correlation between elevated systolic blood pressure and heightened severity of PH. Furthermore, there was a notable correlation between the progression of CKD stages and the heightened severity of pulmonary hypertension (PH). The degree of pulmonary hypertension was found to be higher in individuals who had longer periods of dialysis and in patients with arteriovenous fistulas. Significant associations were seen between greater severity of PH and low haemoglobin levels, elevated serum phosphate levels, increased calcium phosphate product, and elevated intact parathormone levels. Furthermore, those with a low left ventricular ejection fraction (LVEF%) had a greater degree of pulmonary hypertension (PH) severity. The investigations conducted by Zhang *et al*. [17] and K. Ramasubbu *et al*. [18] did not find any significant correlation between the severity of PH and either systolic or diastolic blood pressure. Therefore, although prior studies have linked hypertension to the occurrence of pulmonary hypertension (PH) in individuals with chronic kidney disease (CKD), there is no conclusive evidence of a correlation between hypertension and the severity of PH. After accounting for confounding variables, a multivariate logistic regression analysis revealed that none of the covariates were identified as independent significant risk factors for pulmonary hypertension. Our research also shown a noteworthy correlation between elevated phosphate levels, increased calcium phosphate product, and increased iPTH levels and the severity of PH. Contrarily, Zhang *et al*. [17] found no correlation between calcium, phosphate, and calcium phosphate levels and the severity of PH. However, they did observe that iPTH levels were significantly greater in severe PH compared to mild and moderate PH.

The incidence of pulmonary hypertension (PH) was significantly greater in patients undergoing dialysis, with certain risk variables associated with PH in this population. Prior to this investigation, individuals with congenital heart failure and acute heart failure had been excluded. Nevertheless, subclinical heart failure was prevalent among individuals with end-stage renal disease (ESRD). Possible reasons may include hypertension, excessive salt and water intake, the multifaceted effects of uraemic toxins, and myocardial ischemia. These variables were more common in people with PH. Arteriovenous fistulae (AVF) are often regarded as the most reliable method for accessing hemodialysis (HD) [19]. They cause a rise in venous return, resulting in an accompanying increase in cardiac output, while simultaneously causing a reduction in systemic vascular resistances [20]. LV mass index, low serum albumin and fluid overload were identified as predictors of pulmonary hypertension (PH) in a multivariate model in a study of patients undergoing peritoneal dialysis (PD) [21].

Conclusion

Our analysis revealed a substantial correlation between pulmonary arterial hypertension (PAH) and chronic kidney disease (CKD) patients. Furthermore, we observed that the severity of PAH tends to worsen as renal function deteriorates in CKD cases. Risk

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factors for the development of pulmonary arterial hypertension (PAH) include anaemia, prolonged dialysis duration, hypertension, hyperparathyroidism, AV fistula, elevated calcium phosphate product, and left ventricular failure. Managing these risk variables may mitigate the advancement and intensity of PAH, hence reducing the incidence of illness and death in CKD.

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