



## Pulmonary hypertension: prevalence and risk factors



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### ARTICLE INFO

#### Article history:

Received 7 February 2016

Accepted 2 May 2016

Available online 9 May 2016

#### Keywords:

PAH

Hemodialysis

Prevalence

Risk factors

### ABSTRACT

**Introduction:** Pulmonary arterial hypertension (PAH), defined as a systolic pulmonary artery pressure above 35 mm Hg, is another vascular disease entity recently described in patients receiving hemodialysis. It is a major problem due to its high prevalence and morbidity and mortality. Its pathophysiological mechanism is just known and the strategies for its supported not yet defined.

**Aims:** To determine the prevalence of PAH in our hemodialysis patients and its risk factors.

**Methodology:** Single center descriptive and analytical cross-sectional study, including 111 hemodialysis patients who had benefited from a trans-thoracic cardiac Doppler ultrasound during 2014. A value greater than or equal to 35 mm Hg is considered PAH and classified as follows: mild PAH (35–50 mm Hg), moderate PAH (50–70 mm Hg), and severe pulmonary hypertension (> 70 mm Hg). Patients with a high probability of secondary PAH, especially those with the following history: chronic obstructive pulmonary disease, pulmonary embolism, were not included.

**Results:** The mean age was  $44.3 \pm 14.2$  years. Among the 111 patients, 18 had pulmonary arterial pressure above 35 mm Hg corresponding to 16.22% of PAH prevalence. The average pressure was 45 mm Hg. Of these 18 patients, 11.8% had mild PAH, 3.4% moderate PAH and 0.8% severe PAH. The average hemodialysis duration was significantly associated with PAH ( $p = 0.003$ ); as well as valvular calcification ( $p = 0.000$ ), mitral regurgitation ( $p = 0.001$ ) and tricuspid regurgitation ( $p = 0.002$ ).

**Conclusion:** Primary pulmonary hypertension is a major problem among our hemodialysis because of its high prevalence and its risk factors.

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### 1. Introduction

Pulmonary arterial hypertension (PAH), pulmonary vascular disease, is defined by the elevation of systolic pulmonary arterial pressure above 35 mm Hg measured by cardiac Doppler ultrasound [1]. Besides the classic cardiovascular conditions recognized as one cause of morbidity and mortality in the hemodialysis patients [2], primary PAH whose mechanisms are incompletely known, is another vascular disease entity recently described in chronic kidney disease (CKD) particularly for patients undergoing hemodialysis. It corresponds to 5th subtype of WSPH classification (World Symposium of Pulmonary Hypertension) established in 2008 in Dana Point [3] and updated in 2013 in Nice. [4] Primary pulmonary hypertension is a major problem of hemodialysis patients because of its high prevalence, sometimes reaching 68% [5–8], and by its significant morbidity and mortality [9]. Its pathophysiological mechanism is just known and the strategies for its taken care not yet defined [10–14]. Our study aims to determine the prevalence of PAH in our hemodialysis patients and its risk factors.

#### 1.1. Methodology

This was a single-center descriptive and analytical cross sectional study, single-center, which included 111 patients aged 18 years and over, undergoing hemodialysis for more than six months in dialysis center of Ibn Rochd University Hospital of Casablanca in Morocco, and who had benefited from a trans-thoracic cardiac Doppler ultrasound during 2014. The pulmonary arterial pressure was measured using the echocardiography. A value greater than or equal to 35 mm Hg is considered PAH and classified as follows: mild PAH (35–50 mm Hg), moderate PAH (50–70 mm Hg), and severe pulmonary hypertension (> 70 mm Hg) [15]. Patients with a high probability of secondary PAH, especially those with the following history: chronic obstructive pulmonary disease, pulmonary embolism, congenital heart disease, acute heart failure, moderate or severe valve disease, aortic valve disease or moderate mitral or severe, connectivity, and sleep apnea were not included. Also patients with overload fluid were not included in the study. Sociodemographic, clinical, and laboratory data were obtained from medical records. Verbal consent was obtained from patients. Data were entered and analyzed using the Sphinx software. The comparison of means was performed by the Student's *t* test or the nonparametric

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Mann–Whitney. Comparison of percentages was performed by the Chi2 test or Fisher's exact test. A value of  $p < 0.05$  was considered significant. Multivariate analysis was performed by logistic regression model.

## 2. Results

The average age of our patients was  $44.3 \pm 14.2$  years (range 18–90 years) with a female predominance in 51.4%. The average duration of hemodialysis was  $146 \pm 80$  months (12 years). Chronic glomerulonephritis predominated causal nephropathy (Table 1). Among the 111 patients, 18 had pulmonary arterial pressure above 35 mm Hg corresponding to 16.22% of PAH prevalence. The average pressure was 45 mm Hg (Table 2). Of these 18 patients, 11.8% had mild PAH (35–50 mm Hg), 3.4% moderate PAH (50–70 mm Hg), and 0.8% severe PAH ( $>70$  mm Hg). In multivariate analysis of risk factors (Table 3), the average duration of hemodialysis was significantly associated with PAH ( $p = 0.003$ ); as well as valvular calcification ( $p = 0.000$ ), mitral regurgitation ( $p = 0.001$ ) and tricuspid regurgitation ( $p = 0.002$ ).

## 3. Discussion

The primary PAH of patients receiving hemodialysis, is a recently described disease [1]. Its incidence is still unknown. Its prevalence reported in the literature comes from studies based as ours on the trans thoracic cardiac ultrasound [12]. In our study, the prevalence of PAH estimated at 16.22%. If this prevalence is similar to that reported by Li et al. in China which is 20% [16], it is significantly less compared to that reported in most other studies that are often between 30 and 68% [5–8]. This difference in prevalence between our study and those of the literature would be partly due to the inaccuracy of the method of diagnosis of PAH that is ultrasound because the result of it depends on the operator's experience. However the prevalence of PAH in patients undergoing hemodialysis, overall remains relatively high and this would be multifactorial. Indeed, hemodialysis patient combines many factors involved in the pathophysiology of primary pulmonary hypertension [12]. These factors include uremic toxins, chronic inflammation, endothelial dysfunction, and mineral bone disorders, malnutrition, the phenomena of bioincompatibility [17]. The existence of chronic inflammation in the uremic is well established [17]. Similarly the proliferation of monocytes and proinflammatory mast cells, and T cell dysfunction has been reported [18]. Increased oxidative stress with excessive production of vasoconstrictive substances such as endothelin-1 and angiotensin II, and the reduction of the synthesis of vasodilators such as nitric oxide (NO), all lead to pulmonary endothelial dysfunction which leads to PAH [19].

In our study, the hemodialysis duration was significantly associated with the occurrence of PAH confirming the result of many other [20] studies. This could be explained by the worsening of inflammatory

**Table 2**

Trans-thoracic cardiac Doppler ultrasound data (n = number of patients).

Data	Patients (n = 111)
EF (Average $\pm$ SD), %	$62.5 \pm 10.5$
PAP, n(%)	
PAP $\leq$ 35 mm Hg	93(83.78)
PAP $>$ 35 mm Hg	18(16.22)
Valvular calcification, n(%)	17(15.32)
Mitral regurgitation, n(%)	45(40.54)
Tricuspid regurgitation, n(%)	46(41.44)

EF: ejection fraction; PAP: pulmonary arterial hypertension.

phenomena due to incompatibilities of dialysis membrane [20]. Also, in our patients, valvular calcifications were significantly associated with the occurrence of PAH; which is not the case of data in the literature. Indeed valvular calcifications were previously considered as a major cause of cardiovascular disease [12] such as PAH in patients with CKD. However, all the studies that tried to correlate valvular calcifications with PAH in patients with CKD failed [21]. In our study, the mitral and tricuspid regurgitation were found to be significantly associated with the occurrence of PAH. However there is no consensus to predict the occurrence of PAH on the abnormalities of cardiac ultrasound in CKD [12]. In Fabio et al.'s study in Italy [22] only mitral regurgitation was significantly correlated with PAH in dialysis patients. In the study of Yigla et al. [23], PAH was significantly correlated with valvular disease.

The limitation of our study initially is in its methodology. Indeed for the diagnosis of PAH, right catheterization is the gold standard, so we used the trans thoracic cardiac ultrasound which may under or overestimate the prevalence [12]. Another limitation of our study is that we had not evaluated all aspects including the treatment of PAH patients receiving hemodialysis.

## 4. Conclusion

Primary pulmonary hypertension is not only a reality in our hemodialysis patients, but also appears as a major problem due to its high prevalence and its risk factors which are essentially cardiovascular such as valvular abnormalities. Primary PAH constitute a significant cause of mortality in hemodialysis patients [9]. Hence early detection of these risk factors is needed for adequate care, only way to prevent the onset of PAH.

## Conflicts of interest

None.

**Table 3**

Risk factors of pulmonary arterial hypertension in multivariate analysis.

Data	Patients		P value
	PAP $\leq$ 35 mm Hg n = 93	PAP $>$ 35 mm Hg n = 18	
Age (average $\pm$ SD), year	$44 \pm 13$	$46 \pm 16$	0.710
Sex, %			
Male	47.31	55.56	0.520
Female	52.69	44.44	
Duration of hemodialysis, month	$147 \pm 83$	$142 \pm 74$	0.003
EF (average $\pm$ SD), %	$64.5 \pm 11.5$	$56.3 \pm 9.4$	0.840
Valvular calcification, %	11.83	33.33	0.000
Mitral regurgitation, %	34.41	72.22	0.002
Tricuspid regurgitation, %	34.41	77.78	0.001
PTHi (average $\pm$ SD), pg/ml	$533 \pm 29$	$513 \pm 34$	0.470
Anemia (average $\pm$ SD), g/dl	$10.1 \pm 2.3$	$9.5 \pm 3.5$	0.522
Albuminemia (average $\pm$ SD), g/l	$43.2 \pm 5.1$	$42.3 \pm 6.3$	0.843

EF: ejection fraction; PAP: pulmonary arterial pressure; PTHi: parathormon.

**Table 1**

Epidemiological data (n = number of patients).

Data	Patients (n = 111)
<i>Clinical data</i>	
Age (average $\pm$ SD), year	$44.3 \pm 14.2$
Female sex, n(%)	57(51)
<i>Hemodialysis data</i>	
Hemodialysis duration (average $\pm$ SD), month	$146 \pm 80$
Causal nephropathy, n(%)	
Diabetes	7(6.2)
Chronic glomerulonephritis	19(17.1)
Nephroangiosclerosis	6(5.4)
Unknown nephropathy	50(45.0)
Others	29(26.1)

SD: standard deviation.

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