

Pulmonary Hypertension in Chronic Hemodialysis Patients at Aristide Le Dantec University Hospital

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Abstract

Introduction: Pulmonary hypertension (PH) is defined as high blood pressure in the lungs. It is recently described as a vascular disease entity in chronic kidney disease, particularly for chronic hemodialysis patients. The aims of this study were to determine the prevalence of PH, to describe clinico-biological and morphological characteristics and to identify risk factors associated with PH in hemodialysis patients. **Patients and methods:** This is a cross-sectional, descriptive, and analytical study during a period of 8 months from January 1, 2019, to August 31, 2019, in the hemodialysis center of nephrology department of Aristide Le Dantec Hospital. All chronic hemodialysis patients for more than 3 months and with PH confirmed by cardiac doppler ultrasound were included. **Results:** During the study period, 25/94 patients on chronic hemodialysis, presented with pulmonary hypertension (26.6%). The mean age was 49.3 ± 12.9 years. The sex ratio (M/F) was 0.92. Exertional dyspnea was found in 18 patients (72%). Cardiac auscultation revealed an arrhythmia in 3 patients (12%), augmented second heart sound in 12 patients (48%). On transthoracic doppler ultrasound, pulmonary systolic arterial pressure was on average 51.4 ± 13.2 mmHg. PH was moderate in 13 patients (52%), mild in 9 patients (36%) and severe in 3 patients (12%). The left ventricular ejection fraction was altered in 9 patients (36%). Three patients (12%) had valve calcifications. They were mainly located at aortic valve (8%) and mitral valve (4%). The major risk factors associated to PH in our patients are pathological fractures ($p = 0.023$), aortic calcifications ($p = 0.023$), ischemic heart disease ($p = 0.023$). The duration of hemodialysis represents another favoring factor ($p = 0.042$). Also implicated are arrhythmias ($p = 0.004$), high cardiac index ($p = 0.043$), ventricular dilatation ($p = 0.034$) and left atrial dilation ($p =$

0.015), as well as dilation of the inferior vena cava ($p = 0.048$).

Keywords

Pulmonary Hypertension, Chronic Hemodialysis Patients, Transthoracic Doppler Ultrasound, Dakar

1. Introduction

Pulmonary hypertension (PH) is defined by elevation of systolic pulmonary arterial pressure above 35 mm Hg measured by transthoracic Doppler ultrasound. It is characterized by an increase in pulmonary vascular resistance which can lead to right ventricular failure [1]. Primary PH, whose mechanisms are incompletely known, is a vascular disease entity recently described in chronic kidney disease, for chronic hemodialysis patients. It corresponds to the 5th subtype of WSPH classification (World Symposium of Pulmonary Hypertension) established in 2008 at Dana Point [2] and updated in 2013 at Nice [3]. Primary pulmonary hypertension is a major problem for hemodialysis patients due to its high prevalence, sometimes reaching 68% [4] [5] [6] [7], and its significant morbidity and mortality [8]. The mechanisms are multifactorial and appear to be due to a combination of pre and post capillary mechanisms [9]. The factors often incriminated are represented by advanced age, duration on hemodialysis, volume overload, anemia, arteriovenous fistula, low left ventricular ejection fraction, left heart anomalies, valvular calcifications [10] [11]. Due to the high prevalence of PH in chronic hemodialysis patients, it is necessary to screen for this disorder and minimize its effects. Data from the Maghreb show a prevalence ranging from 10% to 16% in Morocco [11] [12] and 26.3% in Tunisia [13]. To our knowledge, in sub-Saharan Africa, in Senegal in particular, no data on PH in chronic hemodialysis patients by cardiac doppler ultrasound is available. Based on this observation, we conducted this study to determine the prevalence of PH in chronic hemodialysis patients, to describe the clinico-biological and morphological characteristics of these patients and to identify the factors associated with the occurrence of this PH.

2. Patients and Methods

This is a cross-sectional, descriptive, and analytical study over a period of 8 months from January 1, 2019, to August 31, 2019, in the hemodialysis center of the nephrology department of Aristide Le Dantec Hospital. All patients on chronic hemodialysis for more than 3 months and with PH confirmed by cardiac doppler ultrasound were included. Patients with PH before start hemodialysis and those who dialysed temporarily in our center were excluded. Epidemiological data (age, gender, marital status, socio-professional status) hemodialysis parameters (type of vascular access, seniority in hemodialysis, duration and number

of sessions, dry weight and inter-dialytic weight gain), clinical and paraclinical data were studied. The data was collected from the patients' medical files, using an exploitation sheet. All included patients provided written free and informed consent. Transthoracic doppler ultrasound was performed by a cardiologist using an ultrasound scanner equipped with pulsed, continuous and color doppler. The measurements were performed in accordance with the recommendations of the American Society of Echocardiography [14], on patients in the dorsal and left lateral decubitus position, in inter-dialytic period. The diagnostic of pulmonary arterial hypertension was according to 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension [1].

Statistical Analysis

The data collected was then entered into an Epi-info7 database. For the descriptive study, the quantitative parameters of the patients are expressed as mean \pm standard deviation and the qualitative parameters are expressed in number and frequency. The analytical study was made with cross tables. To compare the frequencies, we used Pearson's χ^2 tests or Fischer's two-sided exact test depending on their conditions of applicability with a significance level for a $p \leq 0.05$. To find the risk factors associated with PH, the comparison was made between two groups of hemodialysis patients: those with PH and those without PH.

3. Results

During the study period, 25/94 patients on chronic hemodialysis, had pulmonary arterial hypertension, with a hospital prevalence of 26.6%. The mean age was 49.3 ± 12.9 years [24 and 81 years]. The sex ratio was 0.92, with a slight female predominance (52%). The initial nephropathy was hypertensive nephropathy in 9 patients (36%), it was an undetermined cause in 6 patients (24%) and chronic glomerulonephritis in 5 patients (20%). The mean duration on hemodialysis was 75 ± 40.9 months (Table 1). The vascular access was an arteriovenous fistula in 20 patients (80%). Exertional dyspnea was found in 18 patients (72%). Cardiac auscultation revealed an arrhythmia in 3 patients (12%), augmented second heart sound in 12 patients (48%). The other clinical manifestations were dominated by bone pain in 18 patients (72%). Paraclinically, 23 patients were anemic (92%) with a mean hemoglobin value of 8.38 ± 1.89 g/dl. Hypocalcemia was present in 6 patients (24%) and hyperphosphatemia in only one case (4%). Secondary hyperparathyroidism was observed in 20 patients (95.2%). The mean PTHi was 1166 ± 604 ng/l. Mean vitamin D was 28.8 ± 9.1 ng/l (Table 2). A vitamin D deficiency was found in half of the cases (50%). The Kt/V averaged 1.45 ± 0.28 . It was insufficient in 9 patients (34.8%). On electrocardiogram, left ventricular hypertrophy was found in 8 patients (57.1%), left atrial hypertrophy in 5 patients (35.7%) and repolarization disorders in 3 patients (21.4%). There was 1 case (7.5%) of conduction disorders, arrhythmias, and right ventricular hypertrophy (Table 3). On transthoracic Doppler ultrasound,

Table 1. Clinical and dialytic baseline.

Parameters	Results
Epidemiological data	
Prevalence	26.6%
Mean age	49.3 ± 12.9 years
Gender	
Female	n = 13 (52%)
Male	n = 12 (48%)
Initial Nephropathies	
Hypertensive nephropathy	n = 09 (36%)
Renal polycystosis	n = 02 (08%)
Chronic Glomerulonephritis (CGN)	n = 03 (12%)
Chronic tubulo-interstitial nephropathies (CTIN)	n = 03 (12%)
Diabetic nephropathy	n = 02 (08%)
Non-specified	n = 06 (24%)
Dialysis data	
Mean duration	75 ± 40.9 month
Interdialytic weigh gain	2.08 ± 0.94 kg
KT/V	1.45 ± 0.28

Table 2. Biological baseline of patients.

Parameters	Mean
Hemoglobin (g/dl)	8.38 ± 1.89
Ferritinemia (µg/l)	695.8 ± 299
Albuminemia (g/l)	30.9 ± 8.1
Calcemia (mg/l)	88.8 ± 7.1
Phosphatemia (mg/l)	31 ± 11.4
PTH (pg/ml)	1166 ± 604
Vitamin D (ng/l)	28.8 ± 9.1

Table 3. Electrocardiographic characteristics of patients.

Results	N (%)
Left ventricular hypertrophy	08 (57.1)
Left atrial hypertrophy	05 (35.7)
Sub-epicardial ischemia	01 (7.1)
Rhythm disorder	01 (7.1)
Right ventricular hypertrophy	01 (7.1)
Atrio-ventricular block	05 (1.54)

the mean systolic pulmonary arterial pressure was 51.4 ± 13.2 mmHg with extremes of 35 and 87 mmHg. PH was moderate in 13 patients (52%), mild in 9 patients (36%) and severe in 3 patients (12%). The left ventricular ejection frac-

tion was on average $57.6 \pm 13.1\%$, it was altered in 9 patients (36%). Three patients (12%) had valve calcifications. They were mainly located at the aortic valve (8%) and at the mitral valve (4%). The major risk factors associated of PH in our patients are pathological fractures ($p = 0.023$), aortic calcifications ($p = 0.023$), ischemic heart disease ($p = 0.023$). The duration of hemodialysis represents another favoring factor ($p = 0.042$). Also involved are arrhythmias ($p = 0.004$), high cardiac index ($p = 0.043$), ventricular ($p = 0.034$) and left atrial ($p = 0.015$) dilation, as well as dilation of the inferior vena cava ($p = 0.048$) (Table 4).

4. Discussion

The reported prevalence of PH in the literature in hemodialysis patients was 26% - 40%, detected by Doppler ultrasound [15] [16]. In our series, the hospital prevalence of PH in hemodialysis patients was 26.6%. This hospital frequency was higher than that found by Ezziani in Morocco which was 10% [12]. Amor in Tunisia also found a frequency of 26.3%. [13]. In Iran, Miri found a prevalence of 22% [17]. And in the USA, Navaneethan found a higher prevalence than that of our series, 30% - 40% [18]. The frequency of PH in chronic hemodialysis patients in our study was similar to the Tunisian and Iranian study and significantly lower than that carried out in the USA. This could be explained by the different dialysis protocols and the low sampling of African and Middle Eastern studies; compared to the American series whose cohort included 625 cases of PH out of a total of 2959 hemodialysis patients [18]. The sex ratio found in our study was 0.92. This slight female predominance was similar to that found in Morocco, which was 0.94 [19]. The mean age of our patients was 49.3 ± 12.9 years. Ait Faqih e in Morocco found a mean age similar (46 ± 16 years) [19]. In the series of Shen in China, and Fadaii in Iran, the mean ages were respectively 62.3 ± 12.9 years, 63 ± 16 years, [20] [21]. The data in the literature generally agree and find a higher proportion of elderly people on chronic hemodialysis presenting with PH. In our study, the mean PTHi level was 1165.9 ± 604.3 pg/ml

Table 4. Risk factors associated to PAH.

Parameters	P value
Pathological fractures	0.023
Aortic calcifications	0.023
Ischemic heart disease	0.023
Arrhythmia	0.004
High cardiac index	0.043
Ventricular dilation	0.034
Left atrial dilatation	0.015
Inferior vena cava dilatation	0.048
Duration on hemodialysis	0.042

with 95.2% secondary hyperparathyroidism. Ait Faqih found a mean PTHi level of 513 ± 34 pg/ml [19]. Yoo found an average level of 370 pg/ml with extremes [22]. Shen found a level of 270.8 ± 193.1 pg/ml [20]. All these results were relatively lower than in our series. This could be explained by the non-availability and the cost of curative treatments reducing the iPTH such as calcimimetics and by the absence of a dietician for the prevention of hyperparathyroidism. On transthoracic Doppler ultrasound, the average diameter of the left atrium in our study was 39.6 ± 7.4 mm with 58.8% of cases presenting with dilation of the left atrium. Shen and Yoo found respective averages of 41.2 ± 7.2 mm and 46 ± 5.3 mm [20] [22]. According to their studies, dilation of the left atrium was increased in patients with PH compared to patients who did not. Our data were consistent with those in the literature suggesting that PH was associated with an increase of dilation of the left atrium. In our series, the mean systolic diameter of the left ventricle was 33.7 ± 9 mm, increased in 38.9% of cases. In the Chinese and Brazilian series the values were respectively 33.2 ± 7.5 mm and 32 ± 8 mm [22] [23]. In our study, the left ventricular ejection fraction (LVEF) averaged 57.6%. The fraction was altered in 36% of cases. According to Ait Faqih and Fadai, it was respectively $56.3\% \pm 9.4\%$ and $56\% \pm 5\%$, similar to our study [6]. In Shen's and Yoo's series, the mean LVEF was respectively 66% and $72\% \pm 13$, relatively higher than in our series [20] [22]. We did not find any correlation between LVEF and PH. The results of the Maghreb and China series agree with ours. However, the Iranian and Brazilian series [21] [22] agree to associate an altered LVEF with the development of PH. Indeed, it has been proven that most patients with PH on chronic hemodialysis originate from left heart failure [24]. Our results could be explained by the small sampling of our cohort. In our study, valvular calcifications accounted for 12% ($n = 3$) of cases. According to Ait Faqih, there was 33.3% valve calcification [19]. In our series, among patients with moderate PH, 22.2% had aortic calcification and this result was statistically significant. In Ait Faqih's serie, the association was demonstrated between valvular calcification and the development of PH [19]. Our data are consistent with those of the literature [19]. The inferior vena cava was dilated in 28.6% of cases. There was a statistically significant difference between PH severity and inferior vena cava dilation. Indeed, this is associated with a volume overload in chronic hemodialysis patients and when no measures are taken, these patients subsequently develop left ventricular hypertrophy resulting in the appearance of PH.

The main limitation of this study was the small sample size.

5. Conclusion

This study shows the relatively high prevalence of pulmonary hypertension in chronic hemodialysis patients at Aristide Le Dantec University Hospital. Risk factors of PH in this population were clearly identified. These risk factors are mainly cardiac, hence the importance of regular cardiological monitoring for chronic hemodialysis patients.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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