Scientific Research Publishing

Open Journal of Pediatrics, 2023, 13, 649-656
https://www.scirp.org/journal/ojped
ISSN Online: 2160-8776
ISSN Print: 2160-8741

Pulmonary Arterial Hypertension in Congenital Heart Disease with Left-to-Right Shunt: According to a Retrospective Study at Albert Royer's National Children's Hospital Center

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How to cite this paper: Coundoul, A.M., Bop, K., Faye, A.A., Fall, A.L., Ba, I.D. and Faye, P.M. (2023) Pulmonary Arterial Hypertension in Congenital Heart Disease with Left-to-Right Shunt: According to a Retrospective Study at Albert Royer's National Children's Hospital Center. *Open Journal of Pediatrics*, **13**, 649-656.
https://doi.org/10.4236/ojped.2023.135072

Received: January 25, 2023
Accepted: September 2, 2023
Published: September 5, 2023

Abstract

Pulmonary arterial hypertension PAH is a progressive disease characterized by an increase in pulmonary arterial pressure and resistance. It often complicates congenital heart disease with a left-to-right shunt. The objective of this study is to evaluate the evolutionary profile of the pulmonary pressures of children with congenital heart disease with left-to-right shunt and to identify the factors favoring an evolution towards PAH. This is a retrospective, descriptive and analytical study over a period of four years and six months (from January 1, 2016 to June 30, 2020) at the Center National d'Enfant Albert Royer in Dakar on a series of 87 cases. The hospital frequency was 3.98 per thousand, and the incidence of PAH was 9.44%. The sex ratio of 0.74. The average age was 44.76 months. The average time between the onset of symptoms and the diagnosis of heart disease is 78.81 days. Dyspnea was found in 70.11% of cases, the burst of pulmonary B2 was found in 55%. Global heart failure was noted in 39.08% of cases. Cardiomegaly was found in 89.66% and pulmonary hypervascularization was found in 57.72% of cases. CIV was present in 54.02% of cases, followed by PCA in 21.14% and CAVc in 18.39% of cases. furosemide was used in 97.70% of cases and Captopril in 74.71% of cases. Sildenafil was used in 10.34% of patients, and 12.64% of patients benefited from surgical management. Eisenmenger syndrome was found in 12.64% of patients. PAH in these heart diseases is a formidable and frequent complication, due to an increase in precapillary flow. The major improvement in mortality and morbidity is early surgical management, in the first months of life, to prevent pulmonary vascular disease.

Keywords

PAH, Left-to-Right Shunt, Einsenmenger Syndrome

1. Introduction

Pulmonary arterial hypertension PAH is a progressive disease characterized by an increase in pulmonary arterial pressure and resistance. [1] [2]. It is rare with a prevalence of 30 to 50 people per million population worldwide. Its etiologies are multiple, but PAH secondary to heart disease is the most frequent, often due to an increase in precapillary flow in the left-right shunts or to a postcapillary obstacle or even a combination of the two [3]. The importance and the speed of installation of PAH in these heart diseases depend on each type of heart disease but also on certain terrains such as syndromic or chromosomal pathologies such as trisomy 21 [3]. Progress in the pathophysiological understanding of the mechanisms of PAH has been significant in recent years, allowing significant changes in therapeutic management [4], quality of life and vital prognosis. The major improvement in mortality and morbidity is early surgical management. In sub-Saharan Africa, despite this progress in care, we encounter many difficulties, in particular delays in the initial diagnosis of heart disease, and delays in surgical care.

In Senegal, no study has been carried out to date on pulmonary arterial hypertension in congenital heart disease with left-to-right shunt in pediatrics. Thus, we deemed it necessary to carry out this study, the objectives of which were to establish the epidemiological, clinical, paraclinical and therapeutic profile of children with congenital heart disease with left-to-right shunt and to identify the factors favoring an evolution towards PAH.

2. Methodology

This was a retrospective, descriptive and analytical study carried out during the period from January 1, 2016 to June 30, 2020 at the CNHEAR cardiology department.

We included in this study all children aged 0 to 17 years with congenital heart disease with a left-to-right shunt with PAH criteria defined on cardiac Doppler ultrasound, we excluded primary PAH without a left-to-right shunt and those whose records were incomplete. The data was collected from hospital records based on a data collection sheet pre-established for this purpose. The epidemiological, sociodemographic, maternal, obstetrical, clinical, paraclinical and therapeutic parameters were studied. Data were entered using Microsoft software. After manual counting, data entry and analysis were performed using Sphinx software. The tables and figures were produced with Word 2013 and Excel 2012 softwares (**Tables 1-4**).

Table 1. Distribution of children according to functional signs.

Signs	Effective	Percentage (%)
Permanent dyspnea	61	**70.11**
Cough	54	**62.07**
Difficulty suckling	29	**33.33**
Tears	15	**17.24**
Cyanosis	19	**21.84**
Dyspnea on exertion	4	**4.60**
Adynamia	2	**2.30**

Table 2. Distribution according to the results of Doppler echocardiography.

Echocardiography	Effective	Percentage (%)
CIV	37	42.53
CAVc	12	13.79
PCA	10	08.05
CIA	7	42.53
CIA + CIV	5	05.75
CIA + PCA	3	03.45
TAC	3	03.45
CIV + PCA	3	03.45
CAVp	3	03.45
CAVc + PCA	2	02.30
CAVc + OU	2	02.30
OU	2	02.30
CIV + CIA + PCA	2	02.30
CAVp + PCA	1	01.15

Table 3. Distribution of fixed PAH according to age groups.

Age group/Fixed PAH	Effective	Percentage (%)
30 to 60 months	02	18.18
More than 60 months	09	81.81
Total	11	100

Table 4. Distribution of cases according to evolutionary aspects.

Evolution	Effective	Percentage (%)
Death	06	06.90
Survival	81	93.10
Fixed PAH	11	12.64

3. Results

During the study period, 21,835 patients were hospitalized in the CNHEAR, we included 87 of them in our study, so the hospital frequency was 3.98 per thousand.

During this period 822 congenital heart diseases were recorded, the incidence of PAH in congenital heart disease was 9.44%. The sex-ratio of 0.74, in favor of the female sex. The average age was 44.76 months [1 month and 192 months]. The age interval of 3 to 6 months was the most represented with 34.48%. The low socio-economic level was found in 43.68% of cases. In our study, 63.22% of children began to show symptoms before the age of 3 months, 40.23% of heart diseases were diagnosed between 0 to 3 months of life and 32.18% were diagnosed between 3 to 6 months of life. The average time between the onset of symptoms and the diagnosis of heart disease is 78.81 days [24 hours and 5.83 years]. Dyspnea was found in 70.11% of cases, followed by cough in 62.07%, exertional dyspnea 4.60%. Fever was present in 44 patients (50.57%), 36 patients or 41.38% were malnourished. Pallor and altered general condition were present in almost a quarter of our patients. A trisomy 21 phenotype was noted in 20.69% of our patients. Respiratory distress was found in 66.67% of cases. Pulmonary auscultation noted crackles in 40 patients (45.98%), Cardiac auscultation found a heart murmur in 79 patients (90.80%), pulmonary B2 burst was found in 55% of case. 59 patients or 67.82% had tachycardia and global heart failure was found in 34 patients (39.08%). In our study, only five patients benefited from an electrocardiogram recording, which returned to normal in all four patients. Cardiomegaly was found in 89.66% of cases. Pulmonary hypervascularization was found in 45 patients, *i.e.* 57.72%. 11 patients or 12.64% presented with peripheral pulmonary hypovascularization. CIV was present in 47 patients or 54.02% of cases, followed by PCA present in 21 patients or 21.14%, CAVc was found in 16 patients or 18.39% of cases. Thirty-seven patients or 42.53% had a PAPs on admission estimated at more than 60 mmHg with a maximum at 115 mmHg and a minimum at 65 mmHg. Thirty four patients or 39.08% had PAPs between 45 and 60 mmHg. The main medical treatments used were furosemide in 97.70% of cases and Captopril 74.71. Sildenafil was used in 10.34% of patients. 12.64% of patients benefited from surgical treatment. 11 patients or 12.64% of patients developed Eisenmenger syndrome. Eisenmenger syndrome had developed in six patients with CIV, in four patients with complete CAV and in one patient with PCA. 81.81% of patients who progressed to Eisenmenger syndrome or fixed PAH were aged over 60 months (5 years). Dyspnea on exertion regressed in 71.40% of patients on sildenafil. We noted a clear regression of signs of PAH in patients operated on by shunt removal or banding of the pulmonary artery.

We had found a significant correlation between the age of the patients and the evolution of pulmonary arterial hypertension with a $p = 0.026$.

The sex of the patients was not significantly associated with the unfavorable evolution with a "p" which was equal to 0.962. There was a very significant de-

pendence between the severity of the respiratory signs and the unfavorable evolution with a "p" = 0.009.

Cardiovascular signs were not significantly associated with unfavorable outcome with a "p" of 0.94.

4. Discussion

The prevalence of PAH in pediatric patients is not precisely known [2]. In our study, the hospital frequency was 3.98 per thousand. Diop O [5] found a hospital frequency of pulmonary arterial hypertension in pediatrics, in his study on mortality linked to infantile heart disease, of 1.54 per thousand. This hospital frequency is much lower in developed countries [6] [7]. In fact, arterial hypertension is very common in our patients because of late treatment [8]. In a Dutch study, 9.9% of 1148 patients with congenital heart disease were found to have PAH [6]. These results are comparable to our study which found a prevalence of 9.44% of PAH in a population of 822 children with congenital heart disease. Data show that the likelihood of PAH increases with age in patients with cardiac abnormalities [6].

In our study, the average age of patients with PAH secondary to congenital heart disease with a left-to-right shunt was 44.76 months (3.73 years) with extremes of 1 month and 192 months (16 years). A study conducted in Switzerland between 1999 and 2005 on PAH in congenital heart disease found an average age of 3 years with extremes of 0 to 18 years [2]. Another study conducted in the United Kingdom PAH service for children between 2001 and 2006 found an average age of 7.9 years [2].

We note through these studies, a late average age which seems linked to the evolution of the disease. Indeed the importance and the speed of installation of this PAH depend on the size of the shunt, the seat and the type of heart disease but also on the ground. In our study the age group 7 to 9 years was the most represented, similar to the study in the United Kingdom.

Dyspnea was found in 70.11% of cases, followed by cough in 62.07% and exertional dyspnea in 4.60%. Ngom N.K. found dyspnea in 54.2%, Bodian in his study on congenital heart disease in adults found dyspnea in 60% of cases [9]. These functional signs are especially those of congenital heart disease which is often expressed at the age of 1 to 3 months, when the pulmonary resistance decreases and the left-right shunt increases [3]. In our study, respiratory signs were at the forefront, respiratory distress was found in 66.67% of cases. Pulmonary B2 burst was found in 55% of cases. These results are described in the literature [3] [10]. 20.69% of patients in our study had trisomy 21. In his patients with Down syndrome, it has been suggested that PAH develops earlier and more aggressively [11]. In the Belgian national register of patients with Eisenmenger syndrome, 45% of the 91 patients included had Down syndrome [12]. In our series, 57.72% of patients had pulmonary hypervascularization, 12.64%. Nyobé Abé M found 72.35% pulmonary hypervascularization. In our series like many other series in

Africa [13], CIV remained the most common. According to the literature, it remains the most frequent nosological entity of congenital cardiovascular anomalies. It accounts for 30% to 60% of congenital heart disease [13]. It represented 42.23% of our study followed by the CAV in 17.24%, the PCA in 11.49% and finally the CIA in 8.05%. These results are comparable to other African studies; European [13]. Of course, specific treatments for PAH have only been approved for veno-occlusive disease. There is currently no evidence that the drugs available in PAH would be effective in slowing down the rise in pulmonary vascular resistance in aged shunts. No study currently allows us to confirm that an increase in pulmonary vascular resistance can be reversed by the use of specific treatments for PAH in congenital heart disease. In summary, it appears justified to treat symptomatic children by analogy with adult studies and children with Eisenmenger syndrome, although there are no randomized pediatric studies [14]. In our study, sildenafil was used in 10.34% of patients. Only 12.64% of patients received surgical treatment. These results are explained by the fact that surgery for congenital heart disease is recent in Senegal, the delay in consultation and the limited means. Diop, *et al.* report that only 17% of patients have access to surgery [15]. In addition, this surgery is generally palliative in complex heart disease. In fact, banding of the pulmonary artery is an indication of necessity in severe forms pending complete correction [8]. The major improvement in mortality and morbidity of children with severe PAH and heart defects is early surgical management, in the first months of life, to prevent pulmonary vascular disease [14]. Without early surgical repair, approximately one-third of pediatric patients with left-to-right shunt congenital heart disease develop significant PAH [6]. This evolution towards Eisenmenger syndrome was found in 12.64% of cases in our study. These results are explained by the delay in adequate care, 63.63% occurred between 5 and 9 years. Data show that the likelihood of fixed PAH increases with age in patients with cardiac abnormalities. According to a study conducted in the Netherlands, Eisenmenger syndrome was present in 3% of medically treated patients and present in only 1 of 226 patients who underwent surgical closure of the shunt. The rapid onset of PAH and its progression to veno-occlusive disease depend on the size of the shunt and the type of heart disease. Eisenmenger syndrome was more than twice as common in patients with CIV (48%) compared to people with ASD (17%). In our study, 54.54% is secondary to CIV and 36.36% to complete CVA. Interestingly, the onset of Eisenmenger syndrome tends to be early in patients with CIV or CAVc, of which 80% of cases occur during early childhood, whereas in patients with ASD, 90% of cases occur in adulthood [16]. In our study dyspnea on exertion regressed in 71.40% of patients on sildenafil Elaine M. C Chau in a study conducted at Grantham hospital, England showed that after long-term use of sildenafil, functional capacity improved considerably improved in patients with Eisenmenger syndrome as well as in patients followed for idiopathic pulmonary hypertension. Sildenafil significantly improved hemodynamic lung function in Eisenmenger

patients by reducing systolic and mean pulmonary arterial pressure, pulmonary vascular resistance and improving arterial saturation [6].

5. Conclusion

Overall, our study showed that pulmonary arterial hypertension is common in left-to-right shunt congenital heart disease. Its importance and its speed of installation as well as its evolution depend roughly on each type of heart disease but also on an adapted technical platform in order to respond in due time to the need for care. A remarkable advance on the diagnostic and therapeutic level has been achieved. However, there is a gap in the overall care of these patients, if we compare our results with those of developed countries.

Conflicts of Interest

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

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