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Primary Pulmonary Arterial Hypertension in children: A Hospital Based study

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Abstract

Context: *Pediatric Primary pulmonary Arterial hypertension is a rare disease in infants and an important cause of mortality and morbidity. Timely detection and appropriate treatment strategies are challenges in pediatric age group. Treatable causes need to be identified earlier in the course.*

Aim: *To study the clinical presentation, treatment and outcome at discharge in children with Primary Pulmonary Arterial Hypertension.*

Setting and Design: *It is a Time bound retrospective descriptive chart based observational study. Data was collected by reviewing case records in a predesigned, structured proforma of children above 1 month of age with primary pulmonary hypertension from Jan 2017 to July 2018.*

Results: *There were total 12 cases of primary pulmonary arterial hypertension. Mean age of presentation of primary pulmonary hypertension varied between 1½ month to 1½ years. Common symptoms at presentation were hurried breathing, cough, poor feeding. Primary Pulmonary hypertension was not suspected in majority of children at initial assessment because symptoms were variable. 11(92%) presented with signs of cardiac failure. Chest X Rays showed Cardiomegaly in 50% cases and prominent pulmonary conus in 16%. On ECHO, 100% had RA and RV dilatation and severe PAH. 58% children showed Right Ventricular dysfunction. All the cases were treated with Digoxin, Sildenafil, Milrinone. 4(33%) of them were treated with Thiamine in addition. Mortality rate was high (58%), though all children who were administered thiamine have survived.*

Conclusion: *Primary pulmonary hypertension is a rare disease of infancy with atypical presentation. Mortality rate is high. Administration of Thiamine has proved to be beneficial.*

Keywords: *Primary Pulmonary Arterial Hypertension, Right Ventricular dysfunction*

Introduction

Pediatric Primary pulmonary hypertension(PAH) is rare disease in infants and an important cause of mortality and morbidity.[1] Low prevalence of PAH and subtle symptoms which often mimic other more common cardio-respiratory conditions makes diagnosis of PAH difficult.[2] Hence timely detection and appropriate treatment strategies are challenges in pediatric age group. Since high mortality rate is associated with the condition, treatable causes need to be identified earlier in the course. Few studies have proved Thiamine to be beneficial in Exclusively breastfed infants with PAH.[3]

Objectives of the study

To study the clinical presentation, treatment and outcome at discharge in children with Primary Pulmonary Arterial Hypertension.

Materials and Methods

This is a time bound descriptive chart based observational study. Data was collected by reviewing case records in a predesigned, structured proforma in children above 1 month of age with primary pulmonary hypertension from Jan 2017 to July 2018.Data was analysed according to frequency and percentage. Ethical clearance was sought from the hospital ethical committee. Infants>1 month of age with Primary PAH were included in the study. Neonates with structural congenital heart disease and children with Persistent pulmonary Hypertension of newborn were excluded from the study.

Results

There were 12 children with Primary pulmonary hypertension. 83% of them were < 6 months and all of them were exclusively breast fed. Males were (75%) 3 times more affected than females.

8(66%) of the children presented with hurried breathing. 11(92%) presented with signs of cardiac failure. Other symptoms were poor feeding, poor activity, decreased urine output, that is most of them presented in cardiogenic shock. 16% presented with convulsions.(Table 2)

Table 1. Symptoms and signs in children with Primary Pulmonary Arterial Hypertension

Symptoms and signs	
Hurried Breathing	66% (8/12)
Poor feeding/Poor activity	33% (4/12)
Convulsions	16% (2/12)
Signs of cardiac failure and shock	92% (11/12)

50% of the chest Xrays showed cardiomegaly. 16% of Chest X-Rays showed prominent pulmonary conus. (Table 2)

On ECHO, all the children had RA and RV dilatation. Other important observation was that all of them had severe PAH, that is pulmonary pressure was >2/3 of systemic pressure. 58% (7) children had right ventricular dysfunction (Table 3)

Table 2 Chest X Ray and ECHO findings

Investigations	
CHEST X RAY: Cardiomegaly	50% (6/12)
Prominent Pulmonary Conus	16% (2/12)
ECHO: RA and RV Dilatation	100% (12/12)
Severe PAH	100% (12/12)
Right Ventricular dysfunction	58% (7/12)

All the children were treated with Digoxin, Sildenafil and Milrinone. 2(16%) of them required mechanical ventilation. Serum Thiamine diphosphate (TDP) levels were done in 3 infants, which were grossly low (Table 4). Thiamine was administered in 4(33%) of children. All of them improved clinically.

Table 3 Treatment and Survival

Treatment	Post treatment survival
Sildenafil, Milrinone, Digoxin	8% (1/12)
Sildenafil, Milrinone, Digoxin + Thiamine	100% (4/4)

Table 4 Serum thiamine levels in 3 children before administering Thiamine

Patients	Serum thiamine levels
Patient 1	22.6 mcg/dl
Patient 2	12.78mcg/dl
Patient 3	16mcg/dl

Normal thiamine levels: 28 to 85 mcg/dl

Mortality rate was High (59%). Among the children with Right Ventricular Dysfunction, 6(86%) unfortunately expired.

Thiamine was not given to 8 children (66%), 7(87%) of them succumbed.

Discussion

Mean age of presentation among 12 children with Primary pulmonary hypertensionwas 5½ months. Similarly in a study by IB Javed et al, Mean Age of presentation was 2-4 months.[3] 83%of them were below 6 months of age and all of them were exclusively breast fed. Study done by IB Javed et al states that Thiamine responsive pulmonary hypertension is known in exclusively breastfed babies of thiamine deficient mothers.

66% of the children presented with hurried breathing. In a registry study by Beghetti M et al,

dyspnoea and fatigue were the most frequent symptoms in patients with IPAH.[4][2]

In our study, 92% presented with signs of cardiac failure.Thiamine deficiency, causes fall in systemic blood pressure and shock. Clinical picture includes vasoconstriction in skin and kidney, which will provoke cyanosis and acute renal shutdown.[3] To prove that Thiamine diphosphate (TDP) levels were done in 3 infants in our study, which were grossly low thus further confirming our results.

58% of children had right ventricular dysfunction, 6 of them expired. Although changes in the pulmonary vasculature is the primary cause of pulmonary arterial hypertension (PAH), severity of symptoms and survival are strongly associated with right ventricular function, and right heart failure is the main cause of death in patients with PAH.[5]

Mortality rate was High, but all 4 children who were given thiamine, recovered very rapidly clinically. Our study, like the study done by IB Javed et al showed that Breast fed infants with unusually high pulmonary pressures responded to thiamine challenge with prompt resolution of metabolic complications and reversal of pulmonary hypertension. Repeat echocardiography done after 4–6 weeks showed complete resolution of pulmonary hypertension in 86% infants.[3] The only definitive treatment is therapeutic trial of rapid intravenous administration of thiamine, which improves hemodynamic parameters within minutes to hours. In case of high index of suspicion for thiamine deficiency, this approach is the only way to rapidly diagnose suspected Thiamine Responsive PAH.[6]

There were 4 children with Thiamine Responsive Pulmonary Hypertensive, however we did not know the cause of PAH in rest 66% cases. Cause of IPAH is often difficult to find in a critical care setting due to its protean clinical manifestations, low index of suspicion, and lack of readily available emergent blood thiamine levels[6]

To summarise Primary pulmonary hypertension is a rare disease of infancy with atypical presentation. More than 80% of children were below 6 months of age, all of them were on exclusive breast feeds. Administration of Thiamine has proved to be beneficial in subset of infants who were found to be thiamine deficient. Therapeutic trial of thiamine is worth in infants with diagnosis Primary PAH especially ones on exclusive Breast feeds. Blood thiamine levels should be done if possible before treatment.

Limitations

Limitations of the study were that it was a retrospective study, hence reliability is solely based on documentation in case records. It had a Small Sample size. Thiamine levels were not done in all children. Maternal Thiamine levels could not be done.

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