Survival in Paediatric Pulmonary Arterial Hypertension

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ABSTRACT

Introduction: Outcome of paediatric PAH has not been studied in our population. Current study aimed to see the outcome of children over a study period of one year who were diagnosed as pulmonary arterial hypertension.

Material and Methods: Study was done on all children 0-15 years age diagnosed with PAH on Transthoracic Echocardiography with systolic pulmonary artery pressure (sPAP) of >35 mmHg. Only Group 1 PAH (WHO) were included and were followed for 1 year. Various clinical and echocardiographic variables affecting outcome were noted.

Results: Total number of PAH cases were 40. Mean age at the time of diagnosis was 7.3 months. 23 (57.5%) of the PAH patients were females whereas 17 (42.5%) were males. Idiopathic PAH constituted 42.5% of the study group, whereas 50% of the PAH cases were associated with CHD. 7.5% cases were diagnosed as PPHN Out of the total of 40 cases studied 10 patients died representing 25% mortality over 1 year.

Conclusion: Paediatric PAH is associated with high mortality in our population.Those having Right heart failure and Right Ventricular Dysfunction need close follow up.

Keywords: Paediatric PAH, RV Failure

INTRODUCTION

Pulmonary hypertension (PH) is defined by a mean pulmonary artery pressure >25mmHg at rest or >30 mmHg with exercise.[1,2,3,4,5] PAH is a rare disease with estimated prevalence of 15 to 50 cases per 1 million adults.2 PAH is even less common in children, with an estimated prevalence of 10 cases per 1 million children.[6] Treatment options for children with PAH have been extrapolated from adult guidelines. Although the clinical features and course may differ at times between pediatric and adult patients with PAH, however limited data suggest that the use of medications approved for adults favorably affects children with PAH.[7] Recent observational studies have identified prognostic parameters for adults with PAH[8]; however, prognostic indicators in children are poorly understood. A broader description of current clinical characteristics, treatment patterns, and outcomes of childhood PAH is not yet available to inform physicians The prognosis of PAH is poor with approximately 15% mortality on modern therapy.[9] Predictors of poor prognosis include advanced functional class, poor exercise capacity in 6 minute walk test, high RA pressure, significant RV dysfunction, evidence of RV failure, low cardiac index, high elevated BNP and underlying diagnosis of scleroderma.[10] Clearly patients of CHD with PAH have a better prognosis if surgical correction is done early. We conducted this study to study the mid term survival and factors affecting the survival of our paediatric PAH patients

Current research aimed to study the outcome of children over a study period of one year who were diagnosed as pulmonary arterial hypertension.

MATERIAL AND METHODS

Study was done in the Department of Paediatrics, SKIMS Soura, J&K. Study included all children 0-15 years age diagnosed with PAH on Transthoracic Echocardiography with systolic pulmonary artery pressure (sPAP) of >35 mmHg. Only Group 1 PAH (WHO) were included in the study from sep 2009 to nov 2010 and were followed for 1 year. Various clinical and echocardiographic variables affecting outcome included Dyspnea or Tachypnea, Cyanosis, Poor feeding, Features of Right Heart Failure, Syncope/ Presyncope,severity of PAH, Tricuspid Regurgitation, RV enlargement, Systolic Flattening of IVS, RA enlargement, Right Ventricular Systolic Dysfunction, Pulmonary Regurgitation, Thickened IVS.

RESULTS

Total number of PAH cases were 40. Mean age at the time of diagnosis was 7.3 months. 23 (57.5%) of the PAH patients were females whereas 17 (42.5%) were males. Idiopathic PAH constituted 42.5% of the study group, whereas 50% of the PAH cases were associated with CHD. 7.5% cases were diagnosed as PPHN Out of the total of 40 cases studied 10 patients died representing 25% mortality over 1 year. 5 had IPAH, 4 had PAH with CHD and 1 had PPHN (Graph1). Mortality for different types of PAH was as follows: IPAH: 5 out of 17 (29.41%) PAH associated with CHD: 4 out of 20 (20%) PPHN: 1 out of 3 (33%). Overall 1 year survival rate for PAH was 75%. For different types of PAH the survival rates were as follows: IPAH: 70.59% PAH associated with CHD: 80% PPHN: 66.7% as shown in Table 1. The mean systolic Pulmonary Artery Pressure in the study group was 63.17 mmHg. Most of the cases had severe PAH (65%), whereas moderate and mild PAH cases were 25% and 10% respectively After analyzing the various clinico - echocardiographic risk factors associated with mortality, only two factors, features of right heart failure (p value .0001) and

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	Total No.	Death	1yr Survival Rate
IPAH	17	5 (29.41%)	70.59%
PAH with CHD	20	4 (20%)	80%
PPHN	3	1 (33.3%)	66.7%
Total	40	10 (25%)	75%

Table-1: Mortality of PAH Cases

	Total	Death	p value
Irritability	33	7	.47
Dyspnea or Tachypnea	30	10	.09
Cyanosis	28	8	.69
Poor feeding	26	6	.70
Features of Right Heart Failure	14	9	.0001 (Significant)
Syncope/Presyncope	2	-	-
Mild PAH	4	-	-
Moderate PAH	10	3	.67
Severe PAH	26	7	.70
Tricuspid Regurgitation	40	10	-
RV enlargement	38	10	.11
Systolic Flattening of IVS	34	8	.60
RA enlargement	32	8	1.0
Right Ventricular Systolic Dysfunction	28	10	.04 (Significant)
Pulmonary Regurgitation	16	4	1.0
Thickened IVS	14	5	.44

Table-2: Clinico-Echocardiographic Risk Factors Associated With Mortality by Univariate Analysis

evidence of right ventricular systolic dysfunction (p value .04) were found to be statistically significant. Total of 14 patients had clinical features of RV failure, among them 9 patients died(64.2%) (p=0.0001). Among echocardiographic variables 28 patients had RV dysfunction, out of which 10(35.71%)(p=0.04). Details are shown in Table 2

DISCUSSION

During the study period of one year, 10 patients out of 40 diagnosed of PAH died giving an overall mortality of 25%. The overall one year survival rate for PAH was 75%. The one year survival rate for idiopathic PAH was 70.59% and for PAH associated with CHD 80%. D'Alonzo GE, Barst RJ, et al.[11] have documented a one year survival rate of primary pulmonary hypertension as 68% which is consistent with our findings. S Moledina, A A Hislop[12], et al. have reported a one year survival rate of 89% which is significantly higher than the survival rate in our study. This is due to the fact that new advanced modalities of treatment for idiopathic PAH (prostacyclins, sildenafil, bosentan) were used by them which have prolonged the survival rates. These modalities could not be used in most of the patients in our study group due to problems of availability and compliance and high cost of the drugs. The study by D'Alonzo et al[11] was done before the advent of vasodilator therapy, so their survival rates were similar to ours.

Various clinico-echocardiographic risk factors associated with mortality in PAH were studied, viz, irritability, dyspnea or tachypnea, cyanosis, poor feeding, features of right heart failure, syncope/presyncope, mild PAH, moderate PAH, severe PAH, tricuspid regurgitation, RV enlargement, systolic flattening of IVS, RA enlargement, right ventricular systolic dysfunction, pulmonary regurgitation, and thickened IVS. After applying Chi square test, only two factors were found to be statistically significant predictors of mortality in PAH in children, viz, features of right heart failure (p value .0001) and evidence of right ventricular systolic dysfunction (p value .04). These findings are consistent with McLaughlin VV, Presberg KW, et al.[10] who found that the predictors of poor prognosis include advanced functional class, poor exercise capacity in 6 minute walk test, high RA pressure, significant RV dysfunction, evidence of RV failure. Although changes in the pulmonary vasculature are the primary cause of PAH, severity of symptoms, morbidity and survival are strongly associated with right ventricular function, and right heart failure is the main cause of death in patients with PAH.[13-18] Echocardiography and cardiac MRI allow noninvasive evaluation of right ventricular function . Given the importance of the right ventricle in PAH, preservation and improvement of its function are important aspects of therapy; however, there are few data specifically related to it. Simple, reproducible, noninvasive measures of right ventricular function would help to improve the management of patients with PAH, and to provide tools with which to help establish the optimal therapeutic approach to manage not only the effects of the disease on the pulmonary vasculature, but also to support and improve right ventricular function. Effective treatment modalities are needed to be employed for the large burden of idiopathic PAH cases in Kashmir to decrease the high mortality associated with this disease. Also there is need for specialized centers for early treatment of PAH associated with CHD in Kashmir to decrease the

mortality associated with this potentially curable form of PAH.

CONCLUSION

One fourth of study population died at one year follow up. Effective treatment modalities are needed to decrease the high mortality associated with this disease. Also there is need for specialized centers for early treatment of PAH associated with CHD in Kashmir to decrease the mortality associated with this potentially curable form of PAH. Adequate study of pediatric PH will require multicenter collaboration due to the small numbers of patients, multifactorial disease etiologies and practice variability.

REFERENCES

1. Simonneau G, Galie N, Rubin L, et al. Clinical classification of pulmonary arterial hypertension. Journal of the American College of Cardiology Vol. 43,No.2
2. M.K.Park, Pediatric Cardiology for Practitioners 5th ed. 2008; 590-606. Mosby, Elsevier publications.
3. Hatano S, Strasser T, Editors. Primary Pulmonary Hypertension. Report on a WHO Meeting. Geneva: World Health Organization, 1975:7–45.
4. S.G. Haworth. The management of pulmonary hypertension in children. Archives of Disease in Childhood 2008;93;620-625.
5. Recommendations on the management of pulmonary hypertension in clinical practice. Heart 2001;86: i1.
6. Fraisse A, Jais X, Schleich JM, di Filippo S, Maragnes P, Beghetti M, Gressin V, Voisin M, Dauphin C, Clerson P, Godart F, Bonnet D. Characteristics and prospective 2-year follow-up of children with pulmonary arterial hypertension in France. Arch Cardiovasc Dis. 2010;103: 66 –74.
7. Badesch DB, Raskob GE, Elliott CG, Krichman AM, Farber HW, Frost AE, Barst RJ, Benza RL, Liou TG, Turner M, Giles S, Feldkircher K, Miller DP, McGoon MD. Pulmonary arterial hypertension: baseline characteristics from the REVEAL registry. Chest. 2009;137:376 –387.
8. Benza RL, Miller DP, Gomberg-Maitland M, Frantz RP, Foreman AJ, Coffey CS, Frost A, Barst RJ, Badesch DB, Elliott CG, Liou TG, McGoon MD. Predicting survival in pulmonary arterial hypertension: insights from the Registry to Evaluate Early and Long-Term Pulmonary Arterial Hypertension Disease Management (REVEAL). Circulation. 2010;122:164 –172.
9. Thenappan T, Shah SJ, Rich S, Gomberg-Maitland M. A USA-based registry for pulmonary arterial hypertension: 1982-2006. European Respiratory Journal 2007;30:1103-1110.
10. McLaughlin VV, Presberg KW, Doyle RL, et al. Prognosis of pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. Chest. 2004; 126:78S–92S.
11. D'Alonzo GE, Barst RJ, Ayres SM et al. Survival in patients with primary pulmonary hypertension. Results from a national prospective registry. Annals of Internal Medicine. 1991; 115:343-9.
12. S Moledina1, A A Hislop, H Foster et al. Childhood idiopathic pulmonary arterial hypertension: a national cohort study. Heart 2010;96:1401-1406.
13. Beghetti M, Berger RM, Schulze-Neick I, et al. Diagnostic evaluation of paediatric pulmonary hypertension in current clinical practice. Eur Respir J 2013; 42: 689–700.
14. McGoon MD, Miller DP. REVEAL: a contemporary US pulmonary arterial hypertension registry. Eur Respir Rev 2012; 21: 8–18.
15. van Loon RL, Roofthooft MT, Hillege HL, et al. Pediatric pulmonary hypertension in the Netherlands: epidemiology and characterization during the period 1991 to 2005. Circulation 2011; 124: 1755–1764.
16. Berger RM, Beghetti M, Humpl T, et al. Clinical features of paediatric pulmonary hypertension: a registry study. Lancet 2012; 379: 537–546.
17. van Loon RL, Roofthooft MT, Delhaas T, et al. Outcome of pediatric patients with pulmonary arterial hypertension in the era of new medical therapies. Am J Cardiol 2010; 106: 117–124.
18. Moledina S, Hislop AA, Foster H, et al. Childhood idiopathic pulmonary arterial hypertension: a national cohort study. Heart 2010; 96: 1401–1406

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