The Journal of Teachers Association
ISSN 1019-8555 (Print) & ISSN 2408-8854 (Online)
Frequency: Bi-Annual
DOI: https://doi.org/10.70818/taj.v037i02.0338

OPEN ACCESS
Website: www.tajrmc.com
Email: editor@tajrmc.com
Volume-37 | Issue-2 | Jul-Dec 2024

Association of Congenital CMV Infection in Pediatric Pulmonary Hypertension

Syeda Shayla Afroze*[1], Zannat-E-Khuda[2]

[1] Department of Pediatric Cardiology Bangladesh Shishu Hospital & Institute, Dhaka
[2] Senior Scientific Officer, BIRDEM General Hospital, Dhaka

Abstract: ***Background:*** Cytomegalovirus (CMV) is one of the leading causes of congenital infection in developed countries. Paediatric pulmonary hypertension is related with stunted growth, particularly in younger children. Pulmonary hypertension (PH) is a pathophysiologic condition that is typically related to pulmonary, cardiac, or other systemic illnesses. Pulmonary Hypertension can be the consequence of congenital CMV. ***Objective:*** To observed the congenital CMV association Infection in pulmonary hypertension in children. ***Materials and Methods:*** This observational study was included children included pulmonary hypertensive or non-hypertensive were admitted in the Department of Pediatric Cardiology in Bangladesh Shishu Hospital & Institute (BSHI), Dhaka, from 1st January to 31st November 2024. Total 90 patients aged between 1 month to 6 months with acynotic congenital heart disease, pulmonary hypertensive diagnosed by Doppler echocardiography where PAS >30 mm Hg (without any RVOT) or mean PAP >20 mm Hg were included. Among them 45 were pulmonary hypertension group and 45 were no pulmonary hypertension group. ***Results:*** The mean hemoglobin 11.92(±1.85) vs 11.78(±1.63) (p>0.05), ESR were 79.7 ± 35.7 vs 75.1 ± 26.5 (p>0.05), CRP 64.1 ± 54.4 vs 42.3 ± 31.3 (p<0.05), Leukocyte count (×103 cells/μL) 2395.7 (±1492.3) vs 8954.9 (±5867.5) (p<0.05) and platelet count were 89.18 ±47.16 vs 264.7 ±111.28 (p<0.05) were pulmonary hypertension and no pulmonary hypertension group respectively. Significant association was found CMV with Pulmonary hypertension (p <0.001). ***Conclusion:*** Positive correlation is found in pediatric pulmonary hyoertension patient with CMV infection.

Keywords: Congenital CMV, Pulmonary Hypertension, Infection.

Original Research Article

Correspondence:
Dr. Syeda Shayla Afroze
Registrar,
Department of Pediatric Cardiology
Bangladesh Shishu Hospital & Institute,
Dhaka,

How to cite this article:
Afroze SS & Khuda Z; Association of Congenital CMV Infection in Pediatric Pulmonary Hypertension. Taj 2024;37 (2): 382-386

Article history:
Accepted: December 25, 2024
Published: December 31, 2024

Article at a glance:

Study Purpose: *To evaluate the relationship between congenital CMV infection and pulmonary hypertension in pediatric patients.*

Key findings: *A significant association was found between CMV infection and pulmonary hypertension in children, with notable differences in clinical data such as CRP and leukocyte count.*

Newer findings: *The study adds new evidence linking CMV to pulmonary hypertension in children, suggesting CMV screening in cases of unexplained PH.*

Abbreviations: *CMV – Cytomegalovirus, PH – Pulmonary Hypertension, PAS – Pulmonary Artery Systolic Pressure, ESR – Erythrocyte Sedimentation Rate, CRP – C-Reactive Protein.*

INTRODUCTION

Pediatric pulmonary hypertension is associated with impaired growth, especially in younger children. Pulmonary hypertension (PH) is a pathophysiologic condition that is most often secondary to pulmonary, cardiac, or other systemic diseases.[1] Cytomegalovirus (CMV) is one of the most common causes of congenital infection in the developed countries, affecting approximately 1% of all live births. Most of infected infants will remain asymptomatic, but about 10% of infected newborns will have symptomatic disease and 10–15% will develop problems during the first 6 years of life.[2] Cytomegalovirus (CMV) causes intrauterine

infections in 0.67% of neonates, with 12.7% displaying symptoms at birth. CMV can lead to severe multiorgan involvement, and mortality in symptomatic cases is around 30%. Pulmonary complications are rare in infants with CMV.[3] Children with congenital cytomegalovirus infection has been scarcely described. Pulmonary hypertension may be a rare complication in severely symptomatic congenital cytomegalovirus infants. Lung damage and inflammation cost by the virus increased pulmonary vascular resistance (PVR). The elevated PVR coupled with potentially impaired, result in right to left shunting of blood leading to hypoxemia and systemic hypocalcium.[4] The aim of the present study was to evaluate the relationship between CMV, and pulmonary hypertension and functional status among Bangladeshi children.

METHODS

This observational study was included children included pulmonary hypertensive or non-hypertensive were admitted in the Department of Pediatric Cardiology in Bangladesh Shishu Hospital & Institute (BSHI), Dhaka, from 1st January to 31st November 2024. Total 90 patients aged between 1 month to 6 months with congenital heart disease, pulmonary hypertensive diagnosed by Doppler echocardiography where PAS >30 mm Hg or mean PAP >20 mm Hg were included. Among them 45 were pulmonary hypertension group and 45 were no pulmonary hypertension group. Patients who had abnormalities that limited blood flow to the lungs, such as pulmonary stenosis, disorders that limited systemic blood flow such as aortic stenosis, aortic coarctation, mitral stenosis, as well as patients with rheumatic heart disease, cardiomyopathy, and infective endocarditis were excluded. Patient data were obtained from medical history, which included the following possible predictors of pulmonary hypertension: iron deficiency anemia, mitral regurgitation, pneumonia, and heart failure. Blood culture and gastric swab were negative for bacteria and fungi. Because of neonatal bicytopenia, urine was screened for cytomegalovirus (CMV) infection. CMV DNA was detected by PCR in urine sample. Simultaneously, the patient presented jaundice and hepatosplenomegaly. Subjects were randomly selected by pairing with random numbers generated by *SPSS* ver-25. Chi-square tests were done to assess potential predictive factors of pulmonary hypertension, and analyses were continued by Chi-square result of $p<0.05$.

RESULTS

The average age was 2.3 (±1.27) in the pulmonary hypertension group and 2.86 (±1.39) in the non-pulmonary hypertension group. Younger children are more likely to develop pulmonary hypertension ($p < 0.05$). Gender, weight, height, median heart rate, median respiratory rate, mean hemoglobin, mean corpuscular volume, mean corpuscular hemoglobin, and median red cell distribution width were not significantly different across the pulmonary hypertension groups. (Table-1) Table 2 shows the laboratory data among patients according to hypertension status. The mean hemoglobin 11.92(±1.85) vs 11.78(±1.63) ($p>0.05$), ESR were 79.7 ± 35.7 vs 75.1 ± 26.5 ($p>0.05$), CRP 64.1 ± 54.4 vs 42.3 ± 31.3 ($p<0.05$), Leukocyte count (×103 cells/μL) 2395.7 (±1492.3) vs 8954.9 (±5867.5) ($p<0.05$) and platelet count were 89.18 ±47.16 vs 264.7 ±111.28 ($p<0.05$) were pulmonary hypertension and no pulmonary hypertension group respectively. Table 3 showed significant association was found CMV with pulmonary hypertension ($p <0.001$).

Table 1: Basic characteristics of subjects (N=90)

Characteristics	Study group		p value
	Pulmonary hypertension, n=45	No pulmonary hypertension, n=45	
Age in months	2.3 (±1.27)	2.86 (±1.39)	0.002
Sex			
Male	17 (37.77)	21 (46.67)	0.12
Female	28 (62.22)	24 (53.33)	
Median weight in kg	6.91 (±3.48)	7.68 (±4.59)	0.26
Height	97.41 (±31.7)	98.71(±31.4)	0.80

Median heart rate (IQR), times/minute	115.26 (±37.25)	114.93 (±29.67)	0.95
Median respiratory rate (IQR), times/minute	31.25(±17.9)	29.31(±11.6)	0.45
Hospital stay (days)	15.76 (±4.27)	14.86 (±6.39)	0.002

Table 2: Clinical and biological data among patients with and without hypertension

Characteristics	Study group		p value
	Pulmonary hypertension, n=45	No pulmonary hypertension, n=45	
Mean hemoglobin gm/dL	11.92(±1.85)	11.78(±1.63)	0.63
ESR (mm/h)	79.7 ± 35.7	75.1 ± 26.5	0.48
CRP (mg/L)	64.1 ± 54.4	42.3 ± 31.3	0.01
Leukocyte count (×103 cells/μL)	2395.7 (±1492.3) (1710–4600)	8954.9 (±5867.5) (2690–32500)	0.02
Platelet count	89.18 ±47.16	264.7 ±111.28	<0.001

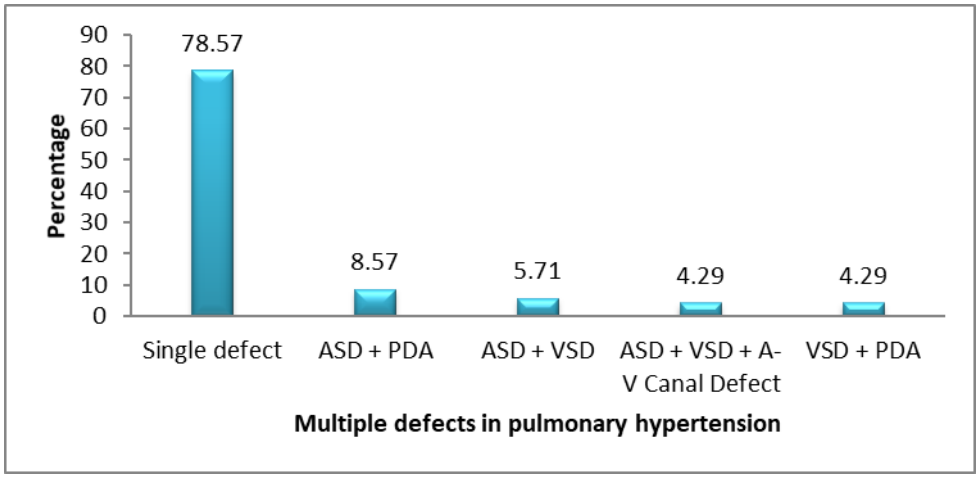

Figure I: Multiple defects in pulmonary hypertension

Table 3: Relation between pulmonary hypertension with CMV

CMV DNA in urine PCR	Study group		p value
	Pulmonary hypertension, n=45	No pulmonary hypertension, n=45	
< 2000 /ml	14 (31.11)	32 (71.11)	<0.001
>2000 /ml	31(68.89)	13 (28.89)	
Total	45 (100.0)	45 (100.0)	

DISCUSSION

The average age was 2.3 (±1.27) in the pulmonary hypertension group and 2.86 (±1.39) in the non-pulmonary hypertension group. Younger children are more likely to develop pulmonary hypertension ($p < 0.05$). Gender, weight, height, median heart rate, median respiratory rate, mean hemoglobin, mean corpuscular volume, mean corpuscular hemoglobin, and median red cell distribution width were not significantly different across the pulmonary hypertension groups. Gunawijaya and Yantie study found that age at presentation were correlated with the correctability of pulmonary hypertension. Infants had more

severe pulmonary hypertension than older children. Females were more prevalent in populations with pulmonary hypertension due to any cause (59%) and in those with PAH-CHD (62%).[5] Barua *et al*., [6] reported the mean ± SD of age was calculated to be, (3.1912 ±3.94387) and age ranged from 25 days to 14 years. About half of the participants [24 (48.0%)] were Males. Male: Female ratio was about 1:1.08 and female were proportionately higher in count.[6]

In this study showed the clinical and biological data among patients according to hypertension status. CRP (mg/L) 64.1 ± 54.4 vs 42.3 ± 31.3 , The mean leukocyte counts 8954.9 (±5867.5) range (2690–32500) *vs* 6395.7 (±5492.3) range (1710–14600) × 103 cells/μL, P = 0.025), and the mean levels of creatinine (1.1 ±0.94 *vs* 0.90 ± 0.51 mg/dL, P = 0.014) were higher in the hypertensive group than in the non-hypertensive group. Similar observation was Jeong et al.[7] study. Arun Babu et al.[8] reported Complete Cell Count (CBC) revealed severe thrombocytopenia and blood serum showed positive Immunoglobulin M (IgM) for CMV and Urinary CMV was positive by nucleic acid test. He was treated with ganciclovir, inhaled nitric oxide and inotropes. He recovered and was discharged on day 24 of life. Severe PHN is a rare manifestation of congenital CMV infection and carries a high risk of morbidity and mortality. Congenital CMV should be considered in neonates with PHN of unknown etiology. Present study showed significant association was found CMV with Pulmonary hypertension (p <0.001). Ong et al.[3] reported the reported pulmonary complications in the case reports were CMV pneumonitis (34.2%), pulmonary hypertension of the newborn (18.4%). Alkoby-Meshulam et al.[4] reported pulmonary hypertension may be a rare complication in severely symptomatic congenital cytomegalovirus infants. It is important to screen for congenital cytomegalovirus in cases of idiopathic refractory pulmonary hypertension. Another Manzoni et al.[9] study also reported neonates with CMV infection associated with severe lung involvement and pulmonary hypertension of the newborn (PHN).

CONCLUSION

In conclusion positive correlation is found in pediatric pulmonary hyoertension patient with CMV infection.

Funding: No funding sources
Conflict of interest: None declared

REFERENCE

1. Mukherjee D, Konduri GG. Pediatric pulmonary hypertension: definitions, mechanisms, diagnosis, and treatment. Comprehensive Physiology. 2021 Jun 30;11(3):2135.
2. Walter-Nicolet E, Leblanc M, Leruez-Ville M, Hubert P, Mitanchez D. Congenital cytomegalovirus infection manifesting as neonatal persistent pulmonary hypertension: report of two cases. Pulmonary Medicine. 2011;2011(1):293285.
3. Ong LT, Fan SW. Pulmonary complications of cytomegalovirus infection in neonates and infants: a systematic review of case reports and pooled analysis. The Pediatric Infectious Disease Journal. 2024 Jun 1;43(6):565-73
4. Alkoby-Meshulam L, Amir J, Lubin D, Klinger G, Guttesman G, Zangen S, Bilavsky E. Congenital cytomegalovirus and pulmonary hypertension. Congenital Anomalies. 2024 Nov;64(6):235-41.
5. Berger RM, Beghetti M, Humpl T, Raskob GE, Ivy DD, Jing ZC, Bonnet D, Schulze-Neick I, Barst RJ. Clinical features of paediatric pulmonary hypertension: a registry study. The Lancet. 2012 Feb 11;379(9815):537-46.
6. Barua C, Barua SK, Hossain MZ, Karim T. Pulmonary hypertension in children with congenital left to right cardiac shunt anomalies. Chattagram Maa-O-Shishu Hospital Medical College Journal. 2015 Nov 16;14(2):31-7..
7. Jeong, S.J., Han, S.H., Kim, C.O., Choi, J.Y., Song, Y.G. and Kim, J.M., 2016. Association between human cytomegalovirus antibody levels, and essential hypertension and functional status in elderly K oreans. Geriatrics & Gerontology International, 16(1), pp.21-27.
8. Arun Babu T, Soliman Y, Mohammad K. Unusual complication of fulminant congenital cytomegalovirus infection. J Neonatal Perinatal Med. 2018;11(2):203-208.
9. Manzoni P, Vivalda M, Mostert M, Priolo C, Galletto P, Gallo E, Stronati M, Gili R, Opramolla A, Calabrese S, Tavella E, Luparia M, Farina D. CMV infection associated with severe lung involvement

and persistent pulmonary hypertension of the newborn (PPHN) in two preterm twin neonates. Early Hum Dev. 2014 Sep;90 Suppl 2:S25-7. doi: 10.1016/S0378-3782(14)50008-4. PMID: 25220122.

The Journal of Teachers Association
Abbreviated Key Title: TAJ
Official Journal of Teachers Association Rajshahi Medical College