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Echocardiographic Study in Preterm Infant with Hemodynamic Significant Patent Ductus Arteriosus

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Abstract

Background: Potential complications of hemodynamic significant patent ductus arteriosus (hsPDA) after birth include heart failure, need for respiratory support, renal disfunction, intraventricular hemorrhage, as well as long term altered growth and development. Nevertheless, clinical signs of patent ductus arteriosus (PDA) are not sensitive and specific enough. Therefore, echocardiography still remains the preferred method to evaluate the ductal patency in preterm infant. The present study aimed to evaluate the echocardiography characteristic in preterm infant with hsPDA.

Methods: A cross-sectional study was conducted on preterm infants aged 3-7 days with 24-33$^{6/7}$ weeks of gestation. Data taken were demographic, clinical and echocardiography. Diagnosis of hsPDA was carried out by echocardiography; defined as >1.5mm diameter of ductus and >1.4 left pulmonal artery and aorta (La/Ao) ratio. The statistical analysis was undertaken using SPSS 21.0.

Results: There were 11 out of 52 preterm infants diagnosed hsPDA. Mean birth weight was 1213±293 gram; Mean gestational age was 30.72±2.01 weeks. In hsPDA group, mean ductus diameter was 2.84±0.93 mm, mean La/Ao ratio was 1.56±0.26, and mean ejection fraction (EF) was 71.55±5.72%.

Conclusion: Echocardiographic evaluation is important for addressing hsPDA in preterm infants.

Keywords: *echocardiographic, preterm infant, hemodynamic significant patent ductus arteriosus*

Introduction

The birth rate of premature babies continues to increase year after year. Complications of preterm birth are still the leading cause of infant mortality, reaching one million deaths in 2015.[1] Patent ductus arteriosus (PDA) is the most common cardiovascular disorder in premature infants.[2] The ducts of arteriosus will normally shrink after birth in a reasonably month-old baby and are functionally closed at the age of 72 hours. The likelihood of spontaneous closure of the ductus arteriosus (DA) in full-term infants without congenital heart disease is very high; but in the preterm infant, closure rates are poorer.[3,4]

Some studies linking uncorrected hsPDA to infant morbidity for less than a month include

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intraventricular bleeding, necrotizing enterocolitis (NEC) and renal insufficiency that can be caused by decreased systemic blood flow and tissue ischemic consequences.[5] Decreased brain oxygenation in infants less than a month can occur in infants with hsPDA resulting in brain damage and developmental disorders.[6] Clinical assessment and echocardiography are reliable methods of diagnosing an hsPDA. Therefore a timely echocardiographic evaluation is needed. The aim of this study was to define the basic functional echocardiographic characteristic of preterm infant with hsPDA.

Methods

A cross-sectional study was conducted in all preterm infants born between November 2019 and May 2020 at the tertiary level neonatal intensive care unit of Dr.Soetomo General Hospital whose oxygen support devices (i.e. high flow nasal canula, continuous positive airway pressure, invasive and non-invasive ventilator) were eligible for inclusion. Patients with multiple congenital anomaly, ductal dependent cyanotic heart defect, early onset of septicemia, and incomplete consent from parents were excluded.

Echocardiography screening was performed between 3rd and 7th postnatal day by pediatric cardiology consultant using Sonoscape Portable Digital Color Doppler Ultrasound System Model S9 (SonoScape, Shenzhen). hsPDA was considered existing if there were a ductus arteriosus with diameter > 1.5 mm on constriction phase, pulmonal perfusion seen in the left pulmonal artery diameter and aorta diameter ratio (LA/Ao) was > 1.4, and left to right shunt were present. While DA that was already closed and did not fulfill the requirement for hsPDA was considered non-hsPDA.

Echocardiographic characteristics of babies with hsPDA were described as mean (M) and standard deviation (SD). Differences in clinical characteristics of the two sample groups of hsPDA and non hsPDA were analyzed using Chi square test, Fisher exact test, and exact probability test. IBM SPSS 21.0 was used for all statistical analyses.

The ethical clearance was issued by the Ethical Committee of Dr. Soetomo General Hospital (No.1766/105/XI/2019). Before the subject recruitment, the researchers had explained to the parents about the general research information and the consent.

Result

Echocardiography evaluation were performed in 52 out of 191 preterm infants treated in NICU during study. Four babies with early onset of septicemia, three babies with multiple congenital anomalies, and babies without complete data and consent were excluded from the study. There were 25 (48%) and 27 (52%) preterm male and female babies, respectively, as shown in Table 1. There were 11 infants meet the criteria of hsPDA based on echocardiography.

Table 1. Subject characteristic

	hsPDA n (11)	**non-hsPDA n (41)**	**Total n (52)**	**P**
Sex Male Female	 5 (9.6) 6 (11.5)	 20 (38.5) 21 (40.4)	 25 (48.1) 27 (51.9)	1.000*
Gestational age *Extremely Preterm* (<28 weeks) *Very Preterm* (28 - <32 weeks) *Moderate Late Preterm* (32 - <37 weeks)	 1 (1.9) 6 (11.5) 4 (7.7)	 3 (5.8) 23 (44.3) 15 (28.8)	 4 (7.7) 29 (55.8) 19 (36.5)	1.000**

Cont... **Table 1. Subject characteristic**

Birth weight ELBW (<1000 g) VLBW (<1500 g) LBW (<2500 g)	 2 (3.9) 7 (13.5) 2 (3.9)	 6 (11.5) 24 (46.1) 11 (21.1)	 8 (15.4) 31 (59.6) 13 (25)	0.902**
Age during recruitment 3 day 4 day 5 day 6 day 7 day	 3 (5.7) 6 (11.5) 1 (1.9) 1 (1.9) 0 (0.0)	 21 (40.5) 10 (19.3) 5 (9.6) 4 (7.7) 1 (1.9)	 24 (46.2) 16 (30.8) 6 (11.5) 5 (9.6) 1 (1.9)	0.118
Infant's comorbidity Respiratory distress synd. Perinatal Asphyxia PPHN Hyperbilirubinemia Others	 6 (11.5) 2 (3.8) 3 (5.7) 4 (7.7) 1 (1.9)	 12 (23.1) 11 (21.1) 3 (5.7) 6 (11.5) 9 (17.3)	 18 (34.6) 13 (24.9) 6 (11.4) 10 (19.2) 10 (19.2)	0.086

Note: Sample characteristic using Chi square test; *Chi squre corrected; **Fisher's exact test

The echocardiography characteristics of hsPDA group research subjects presented in table 2 include ejection fraction (EF), arteriosus duct diameter (DA), left pulmonary artery diameter (La), aortic diameter (Ao), as well as La compared Ao ratio. In determining the status of hsPDA used parameters in the form of DA diameter and La/Ao ratio as a marker of the presence of pulmonary hyperperfusion. In this study obtained the smallest DA diameter of 1.5mm and the largest 4.8mm in the hsPDA group. Of the eleven hsPDA group samples, a diameter of duktus was obtained with an average of 2.84±0.93. The comparison between La and Ao obtained an average score of 1.56±0.26. Ejection fraction in hsPDA group was 71.55±5.72 and the EF in non hsPDA group was 73.94±0.26 (range 56.5-93.12%).

Table 2. Echocardiographic characteristic in hsPDA group

Echocardographic Characteristic	**Patients (n)**	**hsPDA Mean ± SD**
Ejection fraction (%)	11	71.55 ± 5.72
DA diameter (mm)	11	2.84 ± 0.93
Left pulmonary artery diameter (La)	11	11.30 ± 1.97
Aorta diameter (Ao)	11	7.19 ± 1.35
La/Ao ratio	11	1.56 ± 0.26

Discussion

This study showed no significance between gestational age (p = 0.981), birth weight (p = 0.832), single birth of twin mapun (p = 0.322) between hsPDA and non hsPDA groups. Based on gestational age the most to smallest age group was the 28-<32-week group (55.8%), followed by 32-33$^{6/7}$ weeks (36.5%) and gestational age <28 weeks (7.7%). In contrast to other studies where there was an increase in the incidence of hsPDA inversely proportional to the gestational age. Studies in Italy by the Italian Neonatal Network showed higher incidence of PDAs at younger gestational ages: 88.9% and 81.5% at gestational ages of 23 and 24 weeks. PDA incidence decreased at gestation age of 25 weeks by 70.3% and 29 weeks by 32%.[7]

In this study, there were 2/11 neonates with hsPDA having a birth weight of 1000-<1500 grams and as much as 6/41 in the non hsPDA group. The very low birth weight (VLBW) group with a birth weight of 1000-1499 grams in both the hsPDA (7/11) and non hsPDA (24/41) groups had the highest frequency compared to the extremely low birth weight (ELBW, < 1000grams) and low birth weight (LBW, 1500-<2500 grams) groups. These findings are in accordance with previous studies in Palembang, where the majority of babies with PDAs have a birth weight of ≤1500gram and are a risk factor for the occurrence of PDA.[8] Different results were obtained in the study by Su et al., where the incidence of PDA was higher in ELBW (79%) compared to VLBW (65%) neonatal age of 4 days.[9] This difference in proportion can be due to the spread of different samples between birth weight groups where the number of ELBW samples is only 8 infants (15.4%) from the total sample.

The duct of arteriosus normally shrinks after birth in a term infant and is functionally closed at the age of 72 hours. The closure of the ducts was delayed to 4 days in 10% of the babies born with 30 to 37 weeks of gestational age, 80% of babies born gestational age 25 to 28 weeks, and 90% in infants born less than 24 weeks.[3,10] The persistent ductus arteriosus can cause hemodynamic disturbance where the systemic shunt to the pulmonary resulting in pulmonary hyperperfusion and systemic hypoperfusion.[11]

Although ductus arteriosus evaluation is focused on the functional echocardiography, the baby should always undergo a complete echocardiogram first. An initial echocardiogram enables structural congenital heart disease to be excluded. When performing functional echocardiography, it is also important to bear in mind the difficulties and challenges associated with scanning a premature infant. Some babies are very small, they can be agitated or unstable, have a high heart rate, and sometimes a poor echo window, particularly if they are ventilated and have severe underlying lung disease.[4]

In the early hours of life, relatively high pulmonary pressures result in a balanced pulmonary to systemic circulation. A heart murmur, hyperactive precordium, bounding pulses, and a widened systolic to diastolic pulse pressure amplitude are recognized clinical signs attributed to the presence of a hsPDA. Most clinical signs lack sensitivity in the first days of life and hence during this period, a PDA is usually diagnosed by echocardiography.[12] In this study, the pulsation rate between hsPDA and non hsPDA babies is not differ significantly.

This study obtained an average diameter of ductus of 2.84±0.93mm. This result is higher than the study by Visconti et al, in which a spontaneous closed duct with diameter of 1.63mm, ductus that required pharmacological therapy with diameter of 2.24mm, and ductus diameter which require operative therapy of 2.39mm.[13] Determination of hsPDA is generally given when transductal diameter of >1.5mm is obtained. Based on previous studies the value of this intersection indicates the presence of perfusion disorders of the target organ. The La/Ao ratio indicating pulmonary hyper perfusion showed an average value of 1.56±0.26. This figure meets the criteria made by Sehgal and McNamara where the

ducts with an L/Ao ratio of > 1.4±1.6:1 give the effect of moderate hemodynamic disorders on neonates.[14] One baby gave a manifestation of heart failure that was exacerbated by late onset of septicemia that ended in mortality. Three babies in hsPDA group had persistent pulmonary hypertension of the newborn, thus requiring vasodilator treatment prior to ductal closure.

The limitation of this study is focused solely on evaluating the presence of the ductal and left ventricle function. The sample limitation is also a shortcoming in this study. Therefore, future study is needed.

Conclusion

In conclusions, doppler echocardiographic assessment of ductal flow in preterm infant is useful to predict the development of hsPDA. Clinicians need to perform simple echocardiography screening after 3 days of life in preterm infant.

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Ethical Clearance

This study had got permission from the ethics committee of The Faculty of Medicine, Airlangga University Before the subject recruitment, the explanation was done to the parents.

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Conflict of Interest – Nil

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