

## Echocardiographic patterns in asphyxiated neonates

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### Abstract

**Background** Neonatal asphyxia is a disorder in neonates due to decreased oxygenation (hypoxia) and decreased perfusion to organs (ischemia). Duration of asphyxia and early management influence the severity of organ dysfunction, including the heart.

**Objectives** To obtain patterns of cardiac abnormality in neonatal asphyxia in Cipto Mangunkusumo Hospital with echocardiography.

**Design** A cross-sectional study was performed on 22 asphyxiated neonates and 22 other non-asphyxiated neonates from March to October 2008. Inclusion criteria were term neonates, Apgar score  $\leq 6$  in the first minute for asphyxiated neonates and  $\geq 7$  for normal/non-asphyxiated neonate. Echocardiographic examination was performed before the age of 48 hours.

**Results** There were 7/22 asphyxiated neonates and 1/22 non-asphyxiated neonate with heart disease ( $P < 0.05$ ). The most common cardiac abnormality found in asphyxiated neonates was patent ductus arteriosus, followed by atrial septal defect, tricuspid regurgitation, and pulmonary hypertension.

**Conclusion** Cardiac abnormality is significantly found more often in asphyxiated than in non-asphyxiated neonates. [Paediatr Indones. 2009;49:214-18].

**Keywords:** neonatal asphyxia, heart disease, echocardiography

Neonatal asphyxia is still one of the most common cause of mortality and morbidity in developed and developing countries, including in Indonesia.<sup>1,2</sup> The incidence of asphyxia in developed countries is between 1-1.5%, depends on gestational age and birth weight.<sup>3</sup> The

incidence in developing countries is higher than in developed countries due to inadequate antenatal care. Most of these asphyxiated neonates do not receive appropriate management, resulting in high mortality rate.<sup>1,2</sup> With asphyxia incidence of 3-5%, there are estimated 250,000 asphyxiated neonates born each year.<sup>2</sup> In Department of Child Health, Cipto Mangunkusumo Hospital, 6.3% asphyxia neonates were born in the year of 2000, and 21% of those were with severe asphyxia.<sup>4</sup>

Neonatal asphyxia is a disorder due to decreased oxygenation (hypoxia) and decreased perfusion to organs (ischemia).<sup>5,6</sup> In asphyxia state, fetal oxygen supply and fetal heart rate are decreased; therefore oxygen and carbon dioxide interchange in main tissue and organs are also decreased. These conditions result in hypoxemia, accumulation of carbon dioxide, decreased blood pH, and furthermore those will influence various organs, including the heart.<sup>7</sup> Organ dysfunction in asphyxiated neonate depends on duration of asphyxia and early management.<sup>8</sup> Studies on neonatal asphyxia show organ damage in many of them.<sup>7-10</sup> Asphyxiated infants experience blood flow redistribution which provides the heart with more blood flow than other organs. Therefore the heart

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is relatively resistant to hypoxia;<sup>11</sup> however many cardiac abnormality have been observed in neonates with asphyxia.<sup>11-13</sup> We performed a pilot study to determine cardiac status in neonates with asphyxia.

## Methods

This was a cross-sectional study performed in 22 asphyxiated neonates and 22 non-asphyxiated neonates in Perinatology Division, Cipto Mangunkusumo Hospital, from June to October 2008. We included term newborn infant with Apgar score  $\leq 6$  in the first minute for asphyxiated group, and term neonates with Apgar score  $\geq 7$  in the first minute for non-asphyxiated group. We excluded babies with congenital malformation, neonates born to mothers who suffered from intrauterine infection, inadequate antenatal care, incomplete data, and disapproval from parents or surrogates.

Newborns who met the inclusion criteria underwent several examinations: anthropometry (birth weight and birth length), gestational age (Ballard score), and physical examination, particularly heart rate and heart examinations. Echocardiography was performed between the ages of 24-48 hours. Approval from the Ethics Committee, Medical School University of Indonesia was obtained.

**Table 1.** Subjects' characteristics

|                 |                   | Asphyxia<br>n = 22 | Non-asphyxia<br>n = 22 |
|-----------------|-------------------|--------------------|------------------------|
| Sex             | Male              | 8                  | 14                     |
|                 | Female            | 14                 | 8                      |
| Gestational age | 37 weeks          | 4                  | 2                      |
|                 | 38 weeks          | 8                  | 11                     |
|                 | 39 weeks          | 1                  | 2                      |
|                 | 40 weeks          | 9                  | 7                      |
| Birth methods   | Spontaneous       | 7                  | 10                     |
|                 | Cesarean section  | 14                 | 10                     |
|                 | Vacuum extraction | 1                  | 2                      |

**Table 2.** Cardiac abnormality detected with echocardiography

| Cardiac abnormality | Asphyxia<br>n = 22 | Non-asphyxia<br>n = 22 | P     | 95%CI        |
|---------------------|--------------------|------------------------|-------|--------------|
| Yes                 | 7                  | 1                      | 0.023 | 1.33 to 3.33 |
| No                  | 15                 | 21                     |       | PR: 2.1      |

## Results

Characteristics of the neonates in this study, including gestational age, sex, and birth methods are shown in **Table 1**.

The mean gestational age was 38.7 weeks in the asphyxiated neonates, and 38.6 in the non-asphyxiated neonates. The means of birth weight in both groups were 2743.2 and 3064.5 gram, in asphyxiated and non-asphyxiated neonates, respectively; while birth length were 48 and 47.6 cm in asphyxiated and non-asphyxiated neonates respectively.

In heart rate examinations, neither bradycardia nor tachycardia was found in both groups. Murmur was only found in 6/22 asphyxiated neonates, of which four neonates were with severe asphyxia, and two neonates with moderate asphyxia. There were no neonates with murmur found in the non-asphyxia group.

In echocardiography examination, cardiac abnormality was found in 7 out of 22 asphyxiated neonates and in only one out of 22 non-asphyxiated neonates. This value show significant difference proportion between the two groups using Fisher test, with P value of 0.023, 95% confidence interval of 1.52 to 3.35, and prevalence ratio (PR) of 2.1 (**Table 2**).

Cardiac abnormality was found more often in severe asphyxia group (4 out of 9 neonates) rather than in mild or moderate asphyxia group (**Table 3**).

This study found that small PDA occurred more often in non-asphyxiated group (10 neonates), while no small PDA was found in severe asphyxia group. Moderate PDA was found in four neonates in severe asphyxia group, 6 neonates in moderate asphyxia group and none in non-asphyxia group.

## Discussion

This was a cross sectional study using convenient sampling method due to time limitation. Most epidemiology studies need larger subjects, while this study had only 22 subjects. A kappa test should be

**Table 3.** Cardiac abnormality and severity of asphyxia

| Echocardiography results               | Non – asphyxia<br>(n = 22) | Asphyxia (n = 22)             |                            |
|--|----------------------------|-------------------------------|----------------------------|
|  |                            | Moderate asphyxia<br>(n = 13) | Severe asphyxia<br>(n = 9) |
| Normal                                 | 21                         | 10                            | 5                          |
| Abnormal                               | 1                          | 3                             | 4                          |
| Moderate PDA                           | -                          | -                             | 1                          |
| Moderate PDA + small ASD + moderate TR | -                          | 1                             | -                          |
| Moderate PDA + small ASD + PH          | -                          | -                             | 1                          |
| Moderate PDA + PFO                     | -                          | 1                             | -                          |
| Moderate PDA + mild TR + PH            | -                          | -                             | 1                          |
| Moderate PDA + TR + PFO                | -                          | -                             | 1                          |
| PFO + TR                               | -                          | 1                             | -                          |
| VSD                                    | 1                          | -                             | -                          |

PDA : Patent ductus arteriosus, ASD: Atrial septal defect, VSD: Ventricular septal defect, PFO: Patent foramen ovale, TR: Tricuspid regurgitation, PH: Pulmonary hypertension

done to reduce bias. In this study female predominance occurred in asphyxia group, while male predominance was found in non-asphyxia group. Gender did not influence the incidence of asphyxia. The incidence of cardiac abnormalities in newborn is 6-10:1000. The incidences of patent ductus arteriosus (PDA) and atrial septal defect (ASD) are higher in female.<sup>14</sup>

Means of birth weight in this study were 2743.2 (SD 338.6) gram for asphyxia group and 3064.5 (SD 479.9) gram for non-asphyxia group. These conditions were lower than previous study done by Karimi *et al*<sup>15</sup> who found that the means of birth weight were 3343 (SD 271) gram for asphyxia group and 3297 (SD 204) gram for non-asphyxia group). The difference is due to higher gestational age in study by Ercan *et al*<sup>15</sup> (39.7 (SD 1.2) and 39.8 (SD 1.4)) compared to this study (38.7 (SD 1.2) and 38.6 (SD 1.0)). Ancel *et al*<sup>16</sup> reported that mean birth weight for asphyxia babies was 3215(SD 490) gram. Mean birth weight in study done by Low *et al*<sup>17</sup> is lower compared to these studies, because of lower gestational age (mean 32.8 weeks). Fourteen out of 22 babies in this study were delivered by caesarean section. This result is in accordance with study by Ancel *et al*<sup>16</sup> (33 out of 72 babies). Some literatures also reported that caesarean section is a risk factor for asphyxia.<sup>18</sup>

In this study, murmur was found in six asphyxia babies with moderate PDA, while none was found in non-asphyxia babies. Some literatures stated that murmur in neonates with left to right shunt is found in 0-20%neontaes by the age of 2 days. Herdy *et*

*al*<sup>13</sup> found that the murmur in asphyxia babies was 50% more frequent than this study. The possible reason is due to lower gestational age and Apgar score ( $\leq 6$ ).

Asphyxia could cause multi-organ disturbances. In asphyxia babies, acute hypoxia redistributes blood flow so that the heart will receive more blood compared to other organs.<sup>11</sup> These changes is happened due to brain and heart vascular resistance reduction.<sup>9</sup>

On this research, the number of cardiac abnormalities was seven out of 22 asphyxia babies. This result is 60% lower than study conducted by Low *et al*.<sup>17</sup> These differences might be caused by the variation of asphyxia criteria and sample. Definition of asphyxia in this study was based on Apgar score while in study conducted by Low *et al*<sup>17</sup> was based on umbilical pH with base excess of more than 12 mmol and mean pH of 7.08. The degree of asphyxia in study conducted by Low *et al*<sup>17</sup> was more severe therefore more cardiac abnormalities were found. The higher probability of having cardiac abnormalities in that study was due to prematurity.

The frequency of cardiac abnormalities in this study was lower than many studies, i.e. in studies conducted by Chistopher *et al*<sup>3</sup> (62%), Barberi *et al*<sup>20</sup> (61.5%), and Hankins *et al*<sup>21</sup> (78%); however, it is in contrast with study conducted by Martin *et al*<sup>16</sup> (28%). This difference is due to difference of design, sample size, and subject's characters such as inclusion criteria, instruments, and asphyxia criteria.

There is significant difference of subject proportion of having cardiac abnormalities between asphyxia group and non-asphyxia group with P value

of 0.023, 95% CI 1.52 to 3.35, and prevalence ratio 2.1. This means asphyxia newborns have risk of having cardiac abnormalities 2.1 times more frequent than non-asphyxia newborns.

This study shows the most frequent cardiac abnormalities found in asphyxia newborns is PDA (six in 22 newborns). This result is similar with study conducted by Herdy *et al*<sup>13</sup> (20 in 90 asphyxia newborns). Deselina *et al*<sup>22</sup> reported the higher incidence of PDA (seven in 11 preterm asphyxia newborns).

PDA closure physiologically happens in the second day until fourth day of life. The conditions that inhibit PDA closure are asphyxia, low birth weight and prematurity.<sup>19</sup> PDA with diameter less than 3 mm is classified as small.<sup>23</sup> In this study this condition is classified as normal because echocardiography were performed in first and second day of life in which normal closure has not occurred yet. Reller *et al*<sup>24</sup> reported that prevalence of PDA closure in the fourth day was 90%, while Evan and Arcel<sup>25</sup> reported that PDA closure at fourth day of age was 95%.

Tricuspid insufficiency is a cardiac abnormality characterized by right ventricle to right atrium blood flow during systolic phase. Tricuspid insufficiency in asphyxia is due to hypoxia that damages the papillary muscle and tricuspid annulus.<sup>26-28</sup> Tricuspid insufficiency was found in two out of nine babies with severe asphyxia, two out of 13 babies with moderate asphyxia, and none found in non asphyxia babies. This result was lower than study done by Barberi *et al*<sup>20</sup> (seven out of 13 babies with severe asphyxia, seven out of 15 babies with moderate asphyxia, and six out of 22 non-asphyxia babies). Herdy *et al*<sup>13</sup> reported that six out of 90 asphyxia babies had tricuspid insufficiency, which was lower than this study. These differences are probably caused by different asphyxia definition and degree in research subject.

In conclusion, cardiac abnormality is significantly found more often in asphyxiated than in non-asphyxiated neonates.

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