

# Risk factors of neonatal mortality of referred babies with birthweight of 1000 - < 2500 grams

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## ABSTRACT

Dian Murni Wardhani; Setya Wandita; Ekawaty Lutfia Haksari - *Risk factors of neonatal mortality of referred babies with birthweight of 1000- < 2500 grams*

**Background:** Almost 16% from all of the total births in the developing countries are low birthweight babies. Low birthweight babies are an important contribution in neonatal mortality and morbidity worldwide, and contribute to almost 70% of the total neonatal deaths. Proportion of the low birthweight babies in the developing countries is 90% of the total low birthweight babies around the world, which is 20 million annually. Mortality of babies weighing 1000- < 2500 grams in Dr. Sardjito Hospital reached 51.4%, and that of referred babies was 74.6%.

**Objectives:** This research was aimed to find out and measure the risk factors that contribute to the mortality of referred low birthweight babies in the neonatal period.

**Methods:** A hospital-based research with case-control study design was done to discover the risk factors that related to the neonatal mortality of the referred babies with birthweight of 1000- < 2500 grams. Data were collected from babies' medical records treated in the Maternal-Perinatal Installation of Dr. Sardjito Hospital in 2005 to 2007. Target population of this research was the mentioned above who died at the age of 0-28 days. Variable analysis to find out the correlation between the risk factors and the mortality used odds ratio (OR), 95% confidence interval (95% CI), and the significance level with Chi-square test. To measure the risk factors that contributed on the mortality multivariate logistic regression analysis was used.

**Result:** This study involved 190 babies (95 cases and 95 control) weighing between 1000 and < 2500 grams, who were referred to Dr. Sardjito Hospital. Several subjects were excluded, 23 babies because of going home on self-request, 24 because of incomplete status, 76 because of severe congenital anomaly, and 34 were extremely low birthweight babies. Sepsis (OR: 5.054, 95%CI 2.433-11.198), HMD (OR: 4.461, 95%CI 1.595-10.497), hypoglycemia (OR: 3.358, 95%CI 1.679-6.715), and hypothermia (OR: 2.221, 95%CI 1.082-4.560) were the risk factors of mortality.

**Conclusion:** Sepsis, HMD, hypoglycemia, and hypothermia increased the mortality risk of babies weighing 1000- < 2500 grams referred to Dr. Sardjito Hospital, Yogyakarta.

**Key words:** low birthweight baby - risk factor - referral - neonatal death

## ABSTRAK

Dian Murni Wardhani; Setya Wandita; Ekawaty Lutfia Haksari - *Faktor risiko mortalitas neonatal bayi yang dirujuk dengan berat lahir 1000- < 2500 gram*

**Latar Belakang:** Sekitar 16% dari seluruh bayi lahir di negara berkembang mempunyai berat lahir rendah. BBLR memberi kontribusi penting pada morbiditas dan mortalitas neonatal di seluruh dunia, dan mencapai 70% kematian neonatus di beberapa negara. Proporsi BBLR di negara berkembang adalah 90% dari 20 juta kelahiran BBLR pertahun di seluruh dunia. Kematian bayi berat 1000- < 2500 g di RS. Dr. Sardjito mencapai 51,4% dan sebagian besar adalah bayi rujukan.

**Tujuan:** Penelitian ini bertujuan untuk mengetahui dan mengukur faktor risiko yang berpengaruh pada kematian bayi berat lahir rendah rujukan pada masa neonatal.

**Metode:** Penelitian ini berbasis rumah sakit dengan desain kasus kontrol. Data diambil dari rekam medis bayi yang dirawat di Instalasi Maternal Perinatal RS. Dr. Sardjito tahun 2005-2007. Populasi target adalah bayi rujukan dengan

berat lahir 1000- < 2500 g yang meninggal pada umur 0-28 hari. Analisis variabel untuk mengefektifkan hubungan antara faktor risiko dan kematian, dengan menggunakan *odds ratio* (OR), 95% *confidence interval* (95% CI) dan tingkat signifikansi dengan uji *Chi-Square*. Untuk menilai faktor risiko yang berpengaruh terhadap kematian, dilakukan analisis regresi logistik multivariat.

**Hasil:** Penelitian ini mengikutsertakan 190 bayi (95 kasus dan 95 kontrol) berat badan antara 1000- < 2500 g yang dirujuk ke RS. Dr. Sardjito. Beberapa subjek dieksklusi, 23 karena pulang atas permintaan sendiri, 24 status tidak lengkap, 76 kelainan bawaan dan 34 bayi berat lahir ekstrem. Sepsis (OR: 5,054 IK 95% 2,433-11,198), HMD (OR: 4,461 IK 95% 1,595-10,497), hipoglikemia (OR: 3,358 IK 95% 1,679-6,715) dan hipotermia (OR: 2,221 IK 95% 1,082-4,560) merupakan faktor risiko kematian

**Simpulan:** Sepsis, HMD, hipoglikemia dan hipotermia meningkatkan risiko kematian bayi dengan berat lahir 1000- < 2500 g yang dirujuk ke RS. Dr. Sardjito Yogyakarta.

## INTRODUCTION

Almost 24 million (19%) of babies were born with low birthweight.<sup>1</sup> At least 17 million of babies are born with low birthweight every year, and almost 16% of all births in the developing countries are low birthweight babies. Low birthweight babies are babies with birthweight less than 2500 grams, irrespective of the etiology and the gestational age.<sup>2</sup> It gives an important contribution to neonatal morbidity and mortality worldwide, and causes 70% neonatal mortality in several countries. Small for gestational age is the most common form of low birthweight babies in the developing countries (> 60%), while in the developed countries the cause is preterm birth.<sup>3,4</sup>

According to WHO (2003), 8.1 million babies died and almost half of it (3.9 million or 48%) occurred in the neonatal period. Mortality rate of babies has declined worldwide, but the neonatal mortality is slowly decreased. Almost two third (2.8 million) of neonatal mortality occurred in the first week of life<sup>5</sup>, and almost all occurred in the developing countries.<sup>4,6</sup> Low birthweight is the most important factor in neonatal death and a quite significant determinant of the mortality of babies and of under-five-year-old.

Proportion of low birthweight babies in the developing countries is 90% of 20 million babies born per year worldwide, and 90% of the death of low birthweight babies occurred in neonatal period.<sup>1</sup> Babies born outside the hospital and referred to Dr. Sardjito Hospital were 40.7% or almost half of the total number of babies born in the hospital. The proportion of low birthweight babies born outside the hospital (39.8%) is bigger than low birthweight babies born in side the hospital (32.1%). The mortality of babies weighing 1000->2500 grams in

perinatal ward was quite high (51.4%) and the mortality of babies born outside the hospital is still high<sup>7</sup>. Distribution of neonatal death mostly occurred in Java and Bali areas (66.7%), particularly in rural areas (58.6%). Based on the age of the babies when they died, 79.4% of deaths occurred in 0 to 7 days, and 20.6% occurred in 8-28 days<sup>8</sup>, while in Dr. Sardjito Hospital, 67.6% death occurred in 0 to 7 days, and 32.4% occurred in 8-28 days.<sup>7</sup>

The disease pattern causing the death showed that the highest proportion the cause of neonatal death in age group 0-7 days are preterm birth and low birthweight (35%), and then birth asphyxia (33.6%). The most common etiology of neonatal death in age group 8-28 days is infection (57.1%) including tetanus, sepsis, pneumonia, diarrhea; and 14.3% are caused by general problems.<sup>8</sup> The main contributor to the death of low birthweight babies are preterm birth, infection, birth asphyxia, hypothermia, and inadequate breastfeeding. In Dr. Sardjito Hospital, the most common etiology of the mortality in perinatal ward are congenital anomaly (29.5%), sepsis (17.1%), hyaline membrane disease (15.5%), asphyxia (12.4%), pneumonia (11.4%), enterocolitis necroticans (4.7%), immaturity (3.6%), encephalitis (0.5%), and others (5.2%).<sup>8</sup>

## METHODS

A hospital-based research with case-control study design was done to discover risk factors that related to the neonatal mortality of the babies who were born weighing 1000-<2500 grams referred to Dr. Sardjito Hospital. The study was conducted in Maternal-Perinatal Installation of Dr. Sardjito Hospital. Target population of this research was the referred low birthweight babies. Achievable

population was babies who were born weighing 1000-2500 grams referred to Dr. Sardjito Hospital and died at 0-28 days old.

Subjects were referred low birthweight babies who were hospitalized in the Maternal-Perinatal Installation of Dr. Sardjito Hospital and met the inclusion and exclusion criteria. Sampling was conducted by consecutive sampling method, where all subjects met inclusion and exclusion criteria were included in this study until the needed sample size was achieved. Samples were taken from medical records of Dr. Sardjito Hospital Yogyakarta with diagnosis of low birthweight babies and very low birthweight babies who were born outside Dr. Sardjito Hospital.

The sample size in this study was determined by assuming that sepsis was the predictor of risk factor of mortality caused by sepsis in low birthweight babies, with  $RR = 2.4$ . With significance level of 0.05 and statistical power of 80%, the minimum sample size of each group was 92. Therefore, this study needed a minimum of 184 samples. Analysis of each variables to find out the relation between risk factors and mortality used odds ratio (OR), 95% confidence interval (95% CI) of the OR, and 0.05 significance level with Chi-square test.

The difference in proportion of both groups was analyzed with Chi-square test. Multivariate

analysis with logistic regression method was used to obtain the best and simplest model that describes the relation between dependent variables and independent variables.

## RESULTS

This study was conducted for 3 months, between January 2008 until March 2008. Samples were taken from medical records of babies hospitalized in The Maternal-Perinatal Installation of Dr. Sardjito Hospital Yogyakarta, from 2005-2007.

There were 540 low birthweight babies referred to Dr. Sardjito Hospital in 2005-2007, and out of these patients it was excluded: 23 patients who went home on self-request, 24 patients with incomplete status, 76 patients with severe congenital anomaly, and 34 babies with extremely low birthweight. After the exclusion, 95 patients weighing 1000-2499 grams who died were chosen, it was consistent with the sample size.

TABLE 1 shows the characteristics of the subjects, based on gender, bodyweight, gestational age, age of the mother, educational level of the mother, referrer, the referrer institution, birth method, birth assistant, and birth location, and it shows that all of the characteristics were balanced in case and control groups.

TABLE 1. Baseline characteristics of the study

Characteristics	Total number (%)	Died (%)	Live (%)
<b>Birthweight</b>			
• 1000-1499 grams	41 (21.5%)	27 (65.9%)	14 (34.1%)
• 1500-2500 grams	149 (78.5%)	68 (45.6%)	81 (54.4%)
<b>Gestational age</b>			
• < 37 weeks	134 (70.5%)	68 (50.7%)	66 (49.3%)
• > 37 weeks	56 (29.5%)	27 (48.2%)	29 (51.8%)
<b>Gender</b>			
• Male	93 (48.9%)	49 (52.7%)	44 (47.3%)
• Female	97 (51.1%)	46 (47.4%)	51 (52.6%)
<b>Age of the mother</b>			
• < 20 years old	18 (9.4%)	11 (61.1%)	7 (38.9%)
• 20-35 years old	141 (74.2%)	70 (49.6%)	71 (50.4%)
• > 35 years old	31 (16.4%)	14 (45.2%)	17 (54.8%)

Characteristics	Total number (%)	Died (%)	Live (%)
<b>Educational level of the mother</b>			
• Not graduated from elementary school	1 (0.5%)	0	1 (100%)
• Graduated from elementary school	21 (11 %)	18 (83.3%)	3 (16.7%)
• Junior high school	41 (21.5%)	20 (48.8%)	21 (51.2%)
• Senior high school	101(53.5%)	51 (50.5%)	50 (49.5%)
• University	29 (13.5%)	9 (31.0%)	20 (69.0%)
<b>Referrer</b>			
• Midwife	61 (32.1%)	31 (50.8%)	30 (49.2%)
• General practitioner	44 (23.1%)	23 (52.3%)	21 (47.7%)
• Obstetrician	13 (7%)	4 (30.7%)	9 (69.3%)
• Pediatrician	72 (37.8%)	37 (51.4%)	35 (48.6%)
<b>Referrer institution</b>			
• Puskesmas	19 (10 %)	8 (42.1%)	11 (57.9%)
• Obstetric clinic	37 (19.4%)	16 (43.2%)	21 (56.8%)
• Private hospital	57 (30%)	29 (50.9%)	28 (49.1%)
• District hospital	37 (19.4%)	22 (59.5%)	15 (50.5%)
• Doctor practice	4 (2.1%)	3 (75%)	1 (25%)
• Midwife practice	36 (19.1%)	22 (61.7%)	14 (38.3%)
<b>Birth method</b>			
• Spontaneous	132 (69.6%)	65 (49.2%)	67 (50.8%)
• Spontaneous with assistance	7 (3.6%)	7 (100%)	0
• Sectio cesarea	51 (26.8%)	23 (45.1%)	28 (54.9%)
<b>Birth helper</b>			
• None	6 (3.1%)	4 (66.7%)	2 (33.3%)
• Traditional midwife	3 (1.5%)	2 (66.7%)	1 (33.3%)
• Midwife	88 (46.3%)	42 (47.7%)	46 (52.3%)
• General practitioner	8 (4.2%)	4 (50%)	4 (50%)
• Obstetrician	85 (44.9%)	43 (50.6%)	42 (49.2%)
<b>Birth location</b>			
• Polindes	4 (2.1%)	4 (100%)	0
• Home	27 (14.2%)	12 (44.4%)	15 (55.6%)
• Obstetric clinic	53 (27.8%)	28 (52.8%)	25 (47.2%)
• Puskesmas	15 (7.8%)	7 (46.7%)	8 (53.3%)
• District hospital	49 (20.3%)	17 (44.7%)	21 (55.3%)
• Private hospital	53 (27.8%)	27 (50.9%)	26 (49.1%)

The statistically significant risk factors were birthweight (OR: 0.435 p 0.022, 95% CI 0.212-0.896), sepsis (OR: 3.672 p 0.000, 95% CI 1.943-6.939), hyaline membrane disease (HMD) (OR:

3.568 p 0.004, 95% CI 1.437-8.859), hypoglycemia (OR: 2.904 p 0.001, 95% CI 1.494-5.642), and hypothermia (OR: 2.549 p 0.003, 95% CI 1.403-4.631) (TABLE 2).

TABLE 2. Risk factors of mortality of referred babies weighing 1000-2500 grams with univariate analysis

Variable	Case (died) N=95		Control (lived) N=95		OR	95% CI	p
	Total number	%	Total number	%			
<b>Birthweight</b>							
• 1000-1499 grams	27	65.9	14	34.1	0.435	(0.212-0.896)	0.022*
• 1500-2500 grams	68	45.6	81	54.4			
<b>Gestational age</b>							
• < 37 weeks	68	50.7	66	49.3	1.107	(0.593-2.065)	0.750
• > 37 weeks	27	48.2	29	51.8			
<b>Asphyxia</b>							
• Asphyxia (+)	15	65.2	8	34.8	2.059	(0.821-5.067)	0.120
• Asphyxia (-)	80	47.9	87	52.1			
<b>Sepsis</b>							
• Sepsis (+)	47	70.1	20	29.9	3.672	(1.943-6.939)	0.000*
• Sepsis (-)	48	39.0	75	61.0			
<b>HMD</b>							
• HMD (+)	21	75.0	7	25.0	3.568	(1.437-8.859)	0.004*
• HMD (-)	74	45.7	88	54.3			
<b>Polycythemia</b>							
• Polycythemia (+)	5	45.5	6	54.5	0.824	(0.243-2.798)	0.756
• Polycythemia (-)	90	50.3	89	49.7			
<b>Hypoglycemia</b>							
• Hypoglycemia (+)	41	66.1	21	33.9	2.904	(1.494-5.642)	0.001*
• Hypoglycemia (-)	39	40.2	59	59.8			
<b>Hypothermia</b>							
• Hypothermia (+)	67	59.3	46	40.7	2.549	(1.403-4.631)	0.003*
• Hypothermia (-)	28	36.4	49	63.6			

Note : \* statistically significant

TABLE 3. Risk factors of mortality of referred babies weighing 1000-2500 grams with multivariate analysis

Variable	OR (95% CI)
Sepsis	4.119 (2.071-8.187)
HMD	3.908 (1.439-10.613)
Hypoglycemia	2.334 (1.224-4.452)
Hypothermia	2.084 (1.064-4.081)

These significant results were analyzed further with multivariate analysis with logistic regression method. TABLE 3 shows the results of multivariate analysis, i.e. sepsis (OR: 4.119, 95% CI 2.071-8.187), HMD (OR: 3.908, 95% CI 1.439-10.613), hypoglycemia (OR: 2.334, 95% CI 1.224-4.452), and hypothermia (OR: 2.084, 95% CI 1.064-4.081).

Analysis was also conducted by classifying the subjects into subgroups, that is birthweight subgroups and gestational age subgroups (TABLE 4). Birthweight was classified into low birthweight

babies with bodyweight of 1500-2499 grams and very low birthweight babies with bodyweight of 1000-1499 grams, while gestational age was classified into term babies with gestational age > 37 weeks and preterm babies with gestational age < 37 weeks.

Analysis of risk factors of mortality based on birthweight subgroups showed that for low birthweight babies, sepsis (OR: 2.316, 95% CI 1.073-4.997) and hypoglycemia (OR: 2.051, 95% CI 1.031-4.079) were significant risk factors (TABLE 5).

Meanwhile analysis of very low birthweight babies subgroups showed that significant risk factors of mortality were sepsis (OR 9.614, 95% CI 1.476-16.605), HMD (OR 4.476, 95% CI 2.025-9.892), hypoglycemia (OR 5.227, 95% CI 1.336-20.450), and hypothermia (OR 7.462, 95% CI 1.212-15.935) (TABLE 5).

TABLE 4. Risk factors of mortality based on birthweight subgroups

Variable	OR (95% CI)		P	
	LBWB*	VLBWB*	LBWB*	VLBWB*
Asphyxia	1.377 (0.486-3.904)	1.519 (1.218-1.893)	0.598	0.090
Sepsis	2.292 (1.075-4.883)	6.944 (1.734-27.810)	0.036+	0.008+
HMD	2.073 (0.740-5.804)	1.069 (1.251-2.068)	0.195	0.021
Polycythemia	0.786 (0.180-3.425)	0.813 (0.068-9.756)	0.748	0.870
Hypoglycemia	2.031 (1.034-3.990)	5.227 (1.336-20.450)	0.043+	0.024+
Hypothermia	1.450 (0.744-2.828)	8.400 (2.062-34.217)	0.310	0.004+

\*LBWB: birthweight 1500-<2500 grams, VLBWB: birthweight 1000-1499 grams.

+ statically significant

TABLE 5. Risk factors of mortality of LBW dan VLBW babies with multivariate analysis

Variable	OR (95% CI)
<b>LBW</b>	
• Sepsis	2.316 (1.073-4.997)
• Hypoglycemia	2.051 (1.031-4.079)
<b>VLBW</b>	
• Sepsis	9.614 (1.476-16.605)
• HMD	4.476 (2.025-9.892)
• Hypoglycemia	5.227 (1.336-20.450)
• Hypothermia	7.462 (1.212-15.935)

Note: LBW: low birthweight babies  
VLBW: very low birthweight babies

TABLE 6. Risk factors of mortality based on gestational age subgroup

Variable	OR (95% CI)		P	
	PB*	TB*	PB*	TB*
Asphyxia	2.103 (0.678-6.525)	1.970 (0.422-9.168)	0.274	0.642
Sepsis	3.730 (1.783-7.802)	3.676 (0.989-13.667)	0.000+	0.044+
HMD	4.167 (1.551-11.192)	1.077 (0.064-18.117)	0.004+	1.000
Polycythemia	1.477 (0.239-9.135)	0.500 (0.084-2.982)	0.673	0.440
Hypoglycemia	5.250 (1.676-16.443)	1.649 (0.811-3.352)	0.007	0.210
Hypothermia	2.827 (1.403-5.696)	2.045 (0.704-5.946)	0.004	0.284

\* PB : preterm babies (gestational age <37 weeks), TB: term babies (gestational age >37 weeks)

+ : statically significant

Analysis was also conducted based on gestational age. In term babies, significant risk factor was sepsis only (OR: 3.676, 95% CI 0.989-13.667), and in preterm babies significant risk factors of mortality were sepsis (OR: 4,942, 95% CI 2.164-11.286), HMD (OR: 7.388, 95% CI 2.439-22.382), and hypothermia (OR: 3.125, 95% CI 1.417-6.891) (TABLE 6).

Multivariate analysis showed that risk factors of mortality of preterm babies are sepsis (OR 4.942, 95% CI 2.164-11.286), HMD (OR 7.388, 95% CI

2.439-22.382), and the least hypothermia (OR 3.125, 95% CI 1.417-6.891) (TABLE 7)

TABLE 7. Risk factors of mortality of preterm babies with multivariate analysis

Variable	OR (95% CI)
Sepsis	4.942 (2.164-11.286)
HMD	7.388 (2.439-22.382)
Hypothermia	3.125 (1.417-6.891)

## DISCUSSION

The mortality rate of low birthweight babies in Dr. Sardjito Hospital in 2005, 2006, and 2007 were 25.6%, 27.9%, and 35.1%, respectively, similar to the mortality rate of preterm babies and low birthweight babies (29.2%)<sup>8</sup>. Statistically significant risk factors in this study were birthweight, sepsis, HMD, hypoglycemia, and hypothermia.

Birthweight is one of the determinant factors in babies to survive<sup>9</sup>, and 29.2% main etiology of mortality occurs in the neonatal period (babies with the age of < 28 days) is preterm in conjunction with low birthweight.<sup>8</sup> In this study, birthweight was a significant risk factor of mortality of babies who were born weighing 1000-<2500 grams referred to Dr. Sardjito Hospital (OR: 0.435, 95% CI 0.212-0.896), similar to the study on factors affecting the mortality of very low birthweight babies in Japan<sup>10</sup> (RR: 0.56), and study on predictor of mortality of very low birthweight babies in India (OR: 0.037).<sup>11</sup> Low birthweight is relatively common related to immaturity of vital organs and inadequate immune response, therefore, complications easily occurred, increasing the morbidity and mortality of low birthweight babies in neonatal period. In this study, the result showed that birthweight might cause mortality in conjunction with other factors, showed by multivariate analysis result (OR: 0.747, 95% CI 0.328-1.700).

Sepsis in this study was also a significant risk factor (OR 4.119, 95% CI 2.071-8.187). Compared with other studies, it was in Papua New Guinea<sup>12</sup> (OR: 0.36), India<sup>10</sup> (OR: 1.73), and Japan<sup>11</sup> (OR: 4.4). Sepsis in neonates may be classified into early onset sepsis (occurred in 72 hours or 3 first days of life), and late onset sepsis (occurs > 3 days). Neutrophil cells or polymorphonuclear cells (PMNs) in neonates have defect in chemotaxis or bacteria killing. The cell attachment on vascular endothelium is decreased, resulting in decreased ability to leave intravascular space to migrate into tissue. In the tissue, PMN cells failed to degranulate. PMNs in neonates are also less easy to change in shapes, so that their ability to move through extracellular matrix to reach infection or inflammation location is decreased. Neutrophil cells storage is easily depleted because of the lack of response of bone marrow, particularly in premature babies. Fetus has the ability

to produce IgM at gestational age of 10 weeks, although IgM at birth is still low, except in babies who are exposed to infection when they were in the uterus. IgG and IgE may be produced in utero, although they are only found in low level in umbilical blood at birth. Most of IgG is obtained from mother during the last trimester. Neonates receive IgA from breast milk that cannot be secreted until 2-5 weeks after birth. Physical and chemical barriers in human body towards infection are available after birth, but the functions are still undeveloped. Skin and mucous membrane is easily damaged in premature babies. Sick neonates and/or premature babies have higher risk because of invasive procedures that penetrate physical barriers towards infection.<sup>13</sup>

HMD events in low birthweight babies, particularly in premature babies, are quite high. Although not all the babies in this study were prematures, the result was statistically significant (OR: 3.908, 95% CI 1.439-10.613). Hyaline membrane disease (HMD) is a group of symptoms caused by lack of surfactant or immaturity of lung structure.<sup>14</sup> HMD may be the result of genetic problem in production of surfactant related to protein. Surfactant decreases surface tension and prevents alveoli from total collapse at exhalation. The decrease in surface tension facilitates the opening of alveoli with lower energy. Without adequate surfactant, alveoli will collapse and will be very difficult to expand. As a result, blood going through the lungs cannot take oxygen and discard carbon dioxide, and therefore oxygen level in the blood is decreased and carbon dioxide level is increased, causing the increase in blood acidity, hypoxia, and ends in death. HMD occurs in 1% of neonates and serves as the cause of mortality in preterm babies.

Hypoglycemia in this study was statistically significant as risk factor of mortality (OR: 2.334, 95% CI 1.224-4.452). It was different from a study by Basu *et al.* where hypoglycemia was insignificant (OR: 0.98). Hypoglycemia is a common problem in low birthweight babies, both in preterm babies who were appropriate for their gestational age, and in babies with intrauterine growth retardation. Preterm babies who are small for gestational age usually suffer from secondary hypoglycemia caused by inadequate nutrition or the decrease in production of hepatic glucose. The babies have decreased glycogen and fat storage that occurred in the third trimester, and immature liver function with low level of glucone-

genic and glycogenolytic enzymes. Preterm babies also have increased metabolic demand from tachypnea, respiratory distress syndrome, hypoxia, hypothermia, or other events increasing the glucose utilization. Meanwhile, babies who are small for gestational age have risk of hypoglycemia, particularly caused by the increase in production of hepatic glucose and the increase in glucose utilization. Babies who are small for gestational age have an increase in energy demand for bigger body mass size and brain, the increase in metabolic rate, and for polycythemia.<sup>15</sup>

This study showed that hypothermia was a risk factor of mortality (OR: 2.804, 95% CI 1.064-4.081). It was comparable with the study by Basu *et al.* (OR: 2.38). Low birthweight babies are predisposed to hypothermia, because the babies have meagre subcutaneous fat, high ratio between body surface area and bodyweight, and decrease in glycogen and brown fat storage. In addition, hypotonic body postures limit their ability to curl up to decrease skin areas exposed to the colder environment.<sup>16</sup>

Sepsis in low birthweight and very low birthweight babies in this study was significant, but in very low birthweight baby subgroup, the confidence interval was wide, it might be that when they were classified into subgroups, sample size included in birthweight 1000-1499 grams was only 21.5% of total sample size. In gestational age subgroups, death caused by sepsis was statistically significant. HMD was a significant risk factor in very low birthweight babies, and in gestational age < 37 weeks (preterm babies) subgroup, consistent with the theory that HMD was the result of surfactant deficiency in premature babies. Hypoglycemia in birthweight subgroups was significant as risk factor of mortality both in low birthweight babies and very low birthweight babies, but in very low birthweight babies, the confidence interval was wide, it might be that when they were classified into birthweight subgroups, sample size of very low birthweight babies was too small. Meanwhile, in gestational age subgroups, it occurred in premature babies only. In low birthweight babies and term babies, hypothermia was not the risk factor of mortality, while in very low birthweight and preterm babies, it was statistically significant.

The limitation of this study was that it was a retrospective study. Therefore, a systematic error that might cause the result of this study was not consistent with the reality, or usually referred as bias. In this study, information and data were obtained from medical records, so that there was a possibility that information of risk factors or confounding factors were not recorded. Validation on the information was sometimes difficult to obtain. Several clinical parameters containing subjectivity (such as the assessment of asphyxia) were difficult to control. A study with a better design is needed.

## CONCLUSION

It was concluded that sepsis, hyaline membrane disease, hypoglycemia, and hypothermia were risk factors of mortality of babies who were born weighing 1000-<2500 grams and referred to Dr. Sardjito Hospital Yogyakarta. Based on birthweight subgroups: risk factors for 1000-<1500 grams were sepsis, HMD, hypoglycemia, and hypothermia, and risk factors for 1500-<2500 grams were sepsis and hypoglycemia. In gestational age subgroups: risk factors for < 37 weeks were sepsis, HMD, and hypothermia, and for > 37 weeks was sepsis.

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