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Neonatal Therapeutic Intervention Scoring System (NTISS) in Rural Country: Mortality and Length of Stay (LOS) Predictive Score in Preterm Infant

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Abstract

Background: Preterm infants need comprehensive management due to high risk of mortality and morbidity. Proper treatment in NICU can decrease the mortality risk in them, but some of them may take long time before they can go home. Neonatal Therapeutic Intervention Scoring System (NTISS) hopefully can be a predictive score for the mortality and Length of stay (LOS) of a preterm infant, yet, it's use is still very limited in Indonesia. The authors aim to analyze NTISS to predict mortality and length of stay of preterm infants in Indonesia.

Method: This retrospective study conducted in March 2017 and collected medical record data of preterm infants treated in NICU from July 2016 - March 2017. The inclusion criteria were infants with gestational age <37 weeks, treated at NICU> 24 hours and complete medical record data. NTISS total scores are collected after 24 hours at the NICU.

Results: A total of 108 infants met the inclusion criteria. The ratio of NTISS scores had an area under the curve (area under curve / AUC) of 0.879 (95% CI 0.259-0.913) with cutoff at 20.2. it had 91.3% and 74.1% in sensitivity and specificity respectively; 48.8% and 96.9% in positive and negative predictive value respectively; positive likelihood ratio 3.52; negative likelihood ratio 0.12; and 77% inaccuracy. There was no correlation between NTISS scores and length of stay (p = 0.084).

Conclusion: NTISS can be used to predict the mortality of preterm infants.

Keywords: *Preterm infant, Neonatal Therapeutic Intervention Scoring System, Mortality, Length of Stay*

Background

Preterm birth has emerged as one of the global burdens due to its mortality and morbidities[1]. While other causes of death, like pneumonia, diarrhea, malaria, and measles, have been declining for the past 2 decades, complications in children with a history of preterm birth are now becoming the leading cause of death in children under 5 years old, with more than 1 million death reported[2]. A preterm infant is defined as any infant born before 38 weeks of gestational age and can be either spontaneous or provider-initiated[3]. Preterm birth can be In 2010, around 15 million infants born before 38 weeks of gestational age[4]. A similar number is also seen in 2012, which is 11.3 % of all birth worldwide[5]. Approximately, 37.6% of those preterm birth occurred in South Asia while 24.3 % occurred in Southeast Asia[6]. A study in Indonesia stated that there is 101 neonatal death of 807 births in 2014-2015 with preterm birth is

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one of the leading causes of death[7].

Although there are more preterm infants that survive than die in the first 30 days of life[5], the survivors will then have to face the risk of many complications, either early or late complications, in the upcoming years. The infant survivors are in preterm infant and are at a high risk of many complications due to functional and anatomical immaturity. Gestational age and birth weight are indeed associated with mortality rate while sex is still debatable[8,9]. Acute complications related to organ immaturity including respiratory distress syndrome, intracranial hemorrhage, necrotizing enterocolitis, and retinopathy of immaturity[4]. Other studies also stated that there is a significant event of morbidities including weakening neurodevelopmental capacities, learning impedance, visual disorder, and secondary effect in long term health[3]. Hypothermia also increases the infant vulnerability[4] and is associated with a higher mortality rate, intraventricular hemorrhage, lung insufficiency, and bleeding[8]. The presence of the complications before age of 1 month is associated with higher mortality rate to neonatal[10]. Therefore, high quality of intensive training is needed to decrease the preterm infant mortality rate[11].

Intensive treatment of neonatal, including surfactant administration and steroid therapy to treat respiratory distress syndrome, can reduce the neonatal mortality rate[12]. The study reported that as neonatal survival has improved, there is also increasing number of babies requiring long-term neonatal care[13]. It is important to predict the length of stay (LOS) of preterm infant in NICU to assess the resource planning, commissioning of services, and aid clinicians in their counseling to parents[13]. However, there is still limited information on research in the area of predicting the LOS. Many factors are associated with LOS of preterm neonatal in the NICU including gestational age, birth weight, APGAR score, sex, cesarian section, and multiple pregnancies. A study stated that better gestational age and birth weight are associated with a reduction of LOS while gestational age is associated with birth weight[14]. Another study reported that survived extreme preterm infants (<25 weeks) have the longest LOS in the NICU, approximately 107-123 days, while preterm infants with the gestational age of 30-31 weeks are 1 month shorter in LOS[13].

Furthermore, Assessment to predict the mortality rate of preterm neonatal in hospitals, especially in NICU, has been vital information to control the healthcare quality, rational resources management, and to be used as standard outcome comparison in every health care[15]. Several scoring systems can assist to predict mortality and morbidity and improve the outcome validity in many hospitals. Neonatal Therapeutic Intervention Scoring System (NTISS) is a modification of Therapeutic Intervention Scoring System (TISS) that is used in adults. NTISS is a therapy-based and severity-based index that can be used as a neonatal severity indicator and resources utilization[16]. The authors aim to analyze the NTISS as predictive scoring system on mortality rate and LOS in a preterm infant treated in NICU.

Methods and Materials

This was a retrospective study that used medical record data of preterm neonatal treated in the Neonatal Intensive Care Unit (NICU) Dr. Soetomo Hospital Surabaya from July 2016 to March 2017. The inclusion criteria were preterm infants with gestational age <37 weeks when born, 24 hours minimum of treatment in NICU, any incomplete data information would be excluded.

We evaluated the gestational age, birth weight, and APGAR score as the indicator of mortality and morbidity risks and also the length of stay in every infant. Then we assessed all 8 parameters in NTISS. Data were collected and analyzed by chi-square/Fischer's exact test. The prognostic value (sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio, negative likelihood ratio, and accuracy) of NTISS were also analyzed with the ROC curve as the cutoff point. The Institutional Review Board had reviewed and approved this study with ethical clearance No: 1574/KEPK/X/2019.

Result

There was a total of 190 data collected. 82 were excluded and 108 met the inclusion criteria. This study subjects were dominated with female sex (61.6 %), moderate preterm (66.7%), < 2500 gram in birth weight (68.5 %), Caesarian delivery (64.8 %), survived after treatment (78.7 %), and NTISS score over 20.5 (60.2 %). There was no notable domination in the APGAR

score. The basic data characteristics were depicted in table 1.

Table 1. Data Characteristic of Subjects

Indicator	Frequency (n)	Percentage (%)
Sex		
Male	42	38.40
Female	66	61.60
Gestational Age		
Extremely preterm (<28 weeks)	8	7.4
Very Preterm (28-32 weeks)	28	25.9
Moderate Preterm (32-<37 weeks)	72	66.7
Birth Weight		
< 1000 gram	10	9.3
< 1500 gram	16	14.8
< 2500 gram	74	68.5
Normal	8	7.4
Mode of Delivery		
Per Vagina	38	35.2
Caesarian	70	64.8
APGAR score		
0-3	38	35.2
4-6	33	30.55
7-10	37	34.25
Length of Stay		
1-10 days	49	45.4
11-20 Days	30	27.8
21-30 Days	19	17.6
31-40 Days	4	3.6
> 40 Days	6	5.6
Outcome		
Survive	85	78.7
Dead	23	21.3
NTISS Score		
≤ 20.5	43	39.8
> 20.5	65	60.2

In Table 2, Fischer's exact and Chi-Square were used to analyze risk factors related to preterm infant mortality. The table showed that every indicator had a significant result. Furthermore, in the prognostic value of NTISS, with cutoff value in 20.5, the NTISS score had 91.3 % sensitivity, 74.1% specificity, 48.8% PPV, 96.9% NPV, 3.52 Positive likelihood ratio, 0.12 Negative likelihood ratio, and 77% accuracy. The ROC curve was depicted in figure 1.

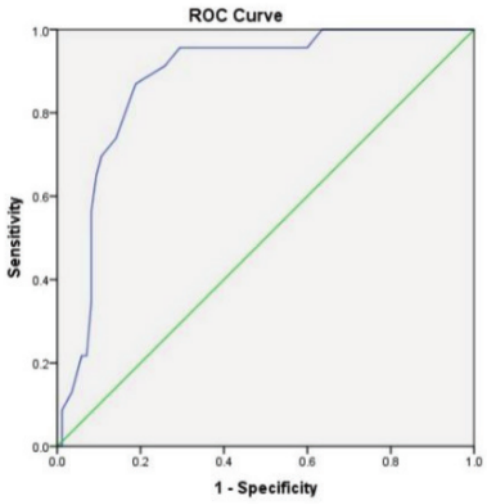

Figure 1. ROC Curve in preterm infants

Table 3 showed the significant correlation between NTISS score and mortality (p= 0.000) in the study while table 4 did not show any significant correlation between NTISS score and length of stay (p= 0.084).

Table 3. Correlation Test Between NTISS and Mortality in Preterm Infant

NTISS Score	Dead	Alive	P	OR
≤ 20.5 > 20.5	2 (3.1 %) 21 (48.8 %)	63 (96.9 %) 22 (51.2 %)	0.000	30 95% CI 6.5-138

Table 4. Correlation Test Between NTISS and Length of Stay

	Length of Stay (Days)					Value	P-Value
	1-10	11-20	21-30	31-40	>40		
NTISS Score ≤ 20.5 > 20.5	31 18	21 9	11 8	1 3	1 5	7.81	0.084
a = Fischer's Exact Test							

Discussion

This study analyzes the mortality risk factors in a preterm infant. Preterm baby and low birth weight had a mortality risk 16 times higher than normal[5]. All extremely preterm is the lowest rate in neonatal survival while moderate preterm is the highest. It shows that higher gestational age is associated with a higher survival rate, similar result also seen in another study[17].

NTISS, as a mortality prediction, is showing a convincing result. A previous study in 2015 stated that

NTISS has 100% in sensitivity and 81.2 % in specificity for mortality prediction with a cutoff point at 28.0 and scoring assessed after 48 hours of treatment[18]. Another study also stated that NTISS is acceptable to be a mortality prediction score, with preterm birth and birth weight between 1000 – 1499 gram as the subject[16]. NTISS shows the number of interventions applied to an infant. The higher NTISS score is, the more interventions are given, thus the mortality rate to the infant is also higher[18]. Surfactant, mechanical ventilation, surgical intervention, and parenteral nutrition administration are the examples of the intervention listed in NTISS. However, some parameters in NTISS were not assessed because they are not performed in the authors' hospital NICU, including aminophylline therapy, extracorporeal membrane oxygenation, pacemaker use, and other cardiac interventions.

Based on the NTISS score got in this study, the respiratory parameter plays a significant role. Most preterm infants that have high respiratory score encounter severe respiratory problems and are at high risk to mortality. The respiratory condition is the most common reason why a newborn infant is treated in NICU, whether term or preterm. Respiratory distress syndrome is the most common diagnosis and the incidence is higher in lower gestational age[19,20]. A study showed that the significance of NTISS variables to predict the mortality risk can be varied because of the birth weight[16]. Another meta-analysis study in 2017 stated that NTISS can be a great predictive tool for mortality and morbidity, but its accuracy is lower in limited resources setting[21].

In this study, the NTISS score is not associated with the length of stay. It means that the total number of interventions given to an infant cannot explain the clinical condition of the infant. LOS of an infant in NICU is affected by gestational age and clinical condition like bronchopulmonary dysplasia (BPD), or persistent apnea. A long treatment in NICU also increases the risk of nosocomial infection[22]. Some studies stated that longer treatment in NICU may be caused by the gestational age, birth weight, intrauterine growth, first 5 minutes of APGAR score, parity, and severe clinical conditions[13,22]. In the conclusion, NTISS can be used as a mortality predictive score in the preterm infant, but its accuracy still needs to be reevaluated and modified, especially in limited resources hospitals where not every parameter in NTISS is available. However, it cannot be used as LOS predictive score for preterm infants. Despite these results, some confounding factors that may affect the result of this study are not evaluated, including congenital abnormalities, history of the mother, and other risk factors that may contribute to longer LOS. Thus, further study with larger samples is needed.

Ethical Clearance was taken from Health Research Ethics Committee RSUD Dr. Soetomo Surabaya, with ethical clearance No: 1574/KEPK/X/2019.

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The authors report no conflict of interest in this work.

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