Original Article

Five-Minute Persistently Low Apgar Score Neonates: The Incidence and Its Risk Characteristics

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Objective: To determine the incidence and risk characteristic of neonates with 5-minute persistently Apgar scores less than or equal to seven in the first and fifth minute.

Materials and Methods: Retrospective case-control study was conducted between January 2014 and December 2015. Both maternal and neonatal medical records were evaluated. Inclusion criteria were singleton gravidas and delivered at gestational age of 28 weeks or more. The neonates with the Apgar score of seven or less in the first minute were included. Known cases of aneuploidy or genetic syndrome, major fetal anomaly, stillbirth, intrauterine fetal death, and incomplete record were excluded. The neonates with an Apgar score of seven or less at the first and fifth minute (LAS-5) were the study group. The neonates whose fifth minute Apgar score were higher than seven (HAS-5) were the control group. Incidence and risk characteristic of neonates with Apgar scores of seven or less in the first and fifth minute with the ones with the same score only in the first minute were measured.

Results: There were 8,141 deliveries during the study period. The final analytic data included 393 neonates. The fifth minute persistently low Apgar score group was 65 neonates (16.5%). Preterm birth, difficult delivery, and non-reassuring fetal heart rate patterns (NRFHR) were independent factors (OR 4.00, 95% CI 2.18 to 7.34; OR 3.91, 95% CI 1.92 to 7.99; OR 3.14, 95% CI 1.58 to 6.21; respectively).

Conclusion: The incidence of LAS-5 was 7.98 per 1,000 live births. Pregnant together with NRFHR, preterm birth, and difficult delivery should be observed closely and prepared for neonatal resuscitation.

Keywords: Apgar score, NRFHR, Preterm birth, Difficult delivery

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Birth asphyxia plays an important role in the maternal and child health issue in the developing countries and contributes to neonatal morbidity and mortality. Prolonged birth asphyxia results in multiple organ systems dysfunction and lead to serious complications, such as epilepsy, cerebral palsy, and developmental delay in the future[1].

Apgar score is used to evaluate the infant's status. It made up from ratings (0, 1, or 2) of five parameters, which are skin color, heart rate, reflex irritability, muscle tone, and respiratory effort. The total score is between 0 and 10 points[2]. Apgar score at first minute is a representative for the requirement of immediate resuscitation, likewise the 5-minute score implies the effectiveness of resuscitative efforts[3]. The previous studies found that a persistently low 5-minute Apgar score group had a higher risk of neurodevelopmental disability than the other group, whose score reached over 7. The reported risks were neonatal seizures, neonatal intracranial hemorrhage, cerebral palsy, mental retardation, and epilepsy[4-6]. Furthermore, some reports mentioned an association between low 5-minute Apgar scores and risk of motor and developmental impairments, including symptoms of attention deficit or speech and language problems[7,8]. From a Uganda study, the rate of neonates with an Apgar score of seven or less at 1-minute after birth who still had an Apgar score of seven or less at 5 minutes (LAS-5) was 2.8% and had

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a significantly higher risk of death[9]. Unfortunately, there is limited data of LAS-5 in the Thai population. The present study aimed to evaluate the incidence and risk characteristics of LAS-5 group among neonate whose 1-minute Apgar score was seven or less in the Prapokklao Hospital's population.

Materials and Methods

Study design and patients

The present study was a retrospective case-control study carried out in the Department of Obstetrics and Gynecology, Prapokklao Hospital, Chanthaburi province, Thailand, and had been approved by the Prapokklao Hospital Research Ethics Committee (reference: CTIREC 026/60). According to the retrospective study working process in the authors hospital, the hospital director authorized the study after the Research Ethic Committee approved the proposal under the ethical issues. The patients' consents were waived because the present study was a retrospective chart review of anonymous patient data. Both maternal and neonate's medical records of singleton pregnant delivered in the hospital between January 2014 and December 2015 were reviewed.

Inclusion and exclusion criteria

Inclusion criteria were singleton gravidas who had a precise gestational age (GA) and delivered at GA of 28 weeks or more. All neonates with the Apgar score 7 or less in first minute were included. Known case of aneuploidy or genetic syndrome, major fetal anomaly, stillbirth, intrauterine fetal death, and incomplete record were excluded.

Clinical outcome definition

The study categorized the data into two groups. The neonates with an Apgar score of seven or less at 1-minute and 5-minute (LAS-5) were defined as the study group. The neonates with 1-minute Apgar score of seven or less and whose 5-minute Apgar score was more than 7 (HAS-5) were defined as the control group.

Risk characteristics

The collected data comprised of antepartum demographic and its clinical characteristics, intrapartum factors, and neonatal outcomes (as showed in Table 1-3).

Sample size calculation

The sample size to achieve 90% power at 5% significance level (two sided) was 192 pregnant woman (32 data for the study group and 160 data for the control group) and to detect the difference of low birth weight (LBW) percentage was 46.2 in the case group and 15.6 in the control group. The ratio of sample size was 1:5 (from pilot study).

Statistical analysis

The continuous variables data were presented as mean with standard deviation and categorical variables as number with percentage. Demographic and risk characteristics were compared using a student t-test, chi-square test, or a Fisher's exact test, as appropriate. Univariate analysis was performed using a simple logistic regression. Multivariate analysis was performed to assess the effect of risk factors. Multiple logistic regressions were used for variables that were found to be significant on univariate analysis. Six variables were sent to the saturated model and four variables remained in the final or reduced model. Risk characteristic with a p-value less than 0.05 was statistical significance. Risk characteristics were expressed as odds ratio with 95% confidence intervals (CI).

Results

There were 8,141 deliveries at Prapokklao Hospital in the study period. After excluding the neonates without birth asphyxia (1-minute Apgar score of 7 or more), 393 neonates were included in the present study. Three hundred twenty-eight (83.5%) cases had only the 1-minute Apgar score of 7 or less, thus were in the HAS-5 group. Sixty-five (16.5%) cases had both the 1-minute and the 5-minute Apgar score of 7 or less, thus were in the LAS-5 group. Mean maternal age of HAS-5 and LAS-5 groups was 26.8±6.5 and 27.8±6.9, respectively (Table 1). Fifty-three cases of HAS-5 group were adolescent (less than 20 years). Seventeen cases in the LAS-5 group were in the advance age group (35 years old or older). The LAS-5 group had lower GA at delivery and lower numbers of term birth in when compared to HAS-5 group (50.8% versus 15.2%, $p<0.001$). The HAS-5 group had lower number of antenatal care (ANC) ($p=0.007$). LAS-5 had mean GA lesser than HAS-1 (36±3.7 versus 38.8±2.6, $p<0.001$). Thirty cases (46.2%) of neonatal birth weight of less than 2,500 grams (LBW) were in LAS-5 group; whereas, there was only three cases (23%) of intrauterine growth restriction (IUGR).

In neonate of GA less than 34 weeks, 18 out of 41 cases were of LBW, and three out of five cases were of IUGR in the LAS-5 group. Neither late preterm nor

Table 1. Antepartum demographic and clinical characteristics

Risk characteristics	HAS-5 (n=328, 83.5%) n (%)	LAS-5 (n=65, 16.5%) n (%)	p-value
Maternal age (years), Mean±SD	26.8±6.5	27.8±6.9	
Maternal age group			0.03
Adolescent (<20 years)	53 (16.2)	5 (7.7)	
Advance age (≥35 years)	47 (14.3)	17 (26.2)	
ANC			
Number of ANC, Mean±SD	7.6±3.2	6.5±3.4	0.007
ANC <5 times	180 (54.9)	25 (38.5)	0.02
Difficult delivery	62 (18.9)	21 (32.3)	0.02
BMI (kg/m^2), Mean±SD	20.39±9.5	21.6±8.6	0.34
Anemic status	54 (16.5)	20 (30.1)	0.014
Medical complication*	60 (18.3)	14 (21.5)	0.602
Abnormal fetal presentation	37 (11.3)	11 (16.9)	0.215
GA at delivery (week), Mean±SD	38.8±2.6	36±3.7	<0.001
Preterm (GA <37 weeks)	50 (15.2)	33 (50.8)	<0.001
IUGR			
Percentile <5	4 (1.2)	1 (1.5)	1
Percentile <10	10 (3.0)	3 (4.6)	0.459

ANC=antenatal care; BMI=body mass index; GA=gestational age; IUGR=intrauterine growth restriction; SD=standard deviation

* Medical complication such as pregnancy induced hypertension, gestational diabetes mellitus, etc.

Table 2. Intrapartum demographic and clinical characteristics

Risk characteristics	HAS-5 (n=328, 83.5%) n (%)	LAS-5 (n=65, 16.5%) n (%)	p-value
MSAF	138 (42.1)	22 (33.8)	0.269
PPROM	32 (9.8)	9 (13.9)	0.372
Oligohydramnios	6 (1.8)	1 (1.5)	1.000
Chorioamnionitis	2 (0.6)	2 (3.1)	0.129
Maternal fever	5 (1.52)	1 (1.5)	1.000
CPD	52 (15.6)	7 (10.8)	0.346
NRFHR	37 (11.3)	18 (27.7)	0.001
Mode of delivery			0.102
Vaginal delivery	132 (40.2)	18 (27.7)	
Cesarean section	143 (43.6)	32 (49.2)	
Operative vaginal delivery	39 (11.9)	11 (16.9)	
Breech assisted delivery	10 (3.0)	4 (6.2)	
Duration (hour), Mean±SD			
First stage of labor	5.3±6	7±6	0.012
Second stage of labor	0.3±6	0.38±7	0.292

MSAF=meconium strained amniotic fluid; PPROM=prolonged premature rupture of membranes; CPD=cephalopelvic disproportion; NRFHR=non-reassuring fetal heart rate patterns; SD=standard deviation

Table 3. Neonatal resuscitation and outcomes

Risk characteristics	HAS-5 (n=328, 83.5%) n (%)	LAS-5 (n=65, 16.5%) n (%)	p-value
Neonatal resuscitation			
PPV	213 (64.9)	60 (92.3)	<0.001
Intubation	25 (7.6)	48 (73.9)	<0.001
Neonatal outcome			
Birth weight (g), Mean±SD	2,989.7±582	2,538±791	0.01
Low birth weight	52 (15.6)	30 (46.2)	<0.001
NICU admission	29 (8.8)	54 (83.1)	<0.001
NICU admission time (day), Mean±SD	0.5±1.6	5.9±8.8	<0.001
Length of stay (day), Mean±SD	5.8±5.1	14±15	<0.001
Respiratory complication	97 (29.6)	58 (89.2)	<0.001
Hypoglycemia	56 (17.1)	34 (53.3)	<0.001
Jaundice	86 (26.2)	47 (72.3)	<0.001
Feeding intolerance	6 (1.8)	7 (10.8)	0.002
Sepsis	16 (4.9)	24 (36.9)	<0.001
Hypovolemic shock	4 (1.2)	15 (23.1)	<0.001
Cardiogenic shock	5 (1.5)	5 (7.7)	0.014
Dead	2 (0.6)	3 (4.6)	0.034

NICU=neonatal intensive care unit; SD=standard deviation

term neonate with IUGR was found in LAS-5 group.

The groups did not show statistical difference in body mass index, medical complications, and fetal presentation. Preterm birth and non-reassuring fetal heart rate patterns (NRFHR) were found more frequently in the LAS-5 group (p<0.001 and 0.001, respectively) (Table 2).

Neonatal resuscitation and outcome of LAS-5 showed a significant higher rate of LBW neonate, positive pressure ventilation (PPV) requirement, intubation, and neonatal intensive care unit (NICU) admission (46.2% versus 15.6%; 92.3% vs. 64.9%; 73.9% versus 7.6%; 83.1 versus 8.8%; respectively). Respiratory complication, neonatal hypoglycemia, neonatal jaundice, feeding intolerance, neonatal sepsis, hypovolemic shock, cardiogenic shock occurred more in the LAS-5 group. LAS-5 also had a significant longer NICU admission time and overall hospital stay. Three babies in the LAS-5 group died during the perinatal period (Table 3). Multivariate statistical analysis of factors associated with LAS-5 is shown in Table 4 and 5. Preterm birth, difficult delivery and NRFHR were risk factors for the LAS-5 group (OR 4.00, 95% CI 2.18 to 7.34; OR 3.91, 95% CI 1.92 to 7.99; OR 3.14, 95% CI 1.58 to 6.21; respectively).

After sub-group analysis in neonate with GA of more than 34 weeks, 348 neonates were persistently exploration (HAS-5=302 versus LAS-5=46), and the result were harmonious with the all population group as shown in Table 3. Risk factors associated with persistently low 5-minute Apgar score were not different to previous analysis in all population groups.

Discussion

Birth asphyxia is one of the public health problems in Thailand. It shares a large majority of perinatal mortality. The Tenth National Economic and Social Development plan aims to control the 1-minute Apgar score of seven or less at under 30 per 1,000 live births[10]. That first minute goal could not be reached in the authors' hospital. A report in 2014 showed that the 1-minute Apgar score of seven or less had a rate of 56 per 1,000 live births in the authors' hospital. LAS-5 indicated that the neonatal was compromised and has a greater risk of neonatal death. The present study data showed three perinatal dead and worse neonatal outcomes in this group. The incidence of the 5-minute persistently low Apgar score neonates in Prapokklao Hospital was 7.98 per 1,000 live births.

Table 4. Univariate analysis of clinical characteristics

Risk characteristics	Odds ratio	95% CI	p-value
Age <20 years	0.50	0.29 to 0.89	0.017
Age ≥35 years	1.92	1.01 to 3.65	0.047
Preterm (<37 weeks)	5.73	3.24 to 10.16	<0.001
ANC <5 times	0.51	0.29 to 0.89	0.017
Medical complication*	1.22	0.64 to 2.36	0.61
Anemic status	2.25	1.23 to 4.12	0.008
Fetal presentation	1.60	0.77 to 3.33	0.208
MSAF	0.70	0.40 to 1.23	0.219
PPROM	1.49	0.67 to 3.28	0.327
NRFHR	3.01	1.59 to 5.72	0.001
Difficult delivery	3.01	1.59 to 5.72	0.001

CI=confidence interval; ANC=antenatal care; MSAF=meconium strained amniotic fluid; PPROM=prolonged premature rupture of membranes; NRFHR=non-reassuring fetal heart rate patterns

* Medical complication such as pregnancy induced hypertension, gestational diabetes mellitus, etc.

Table 5. Multivariate analysis of risk characteristics

Risk characteristics	Odds ratio	95% CI	p-value
NRFHR	3.14	1.58 to 6.21	0.001
Preterm	4.00	2.18 to 7.34	<0.001
Difficult delivery	3.91	1.92 to 7.99	<0.001

CI=confidence interval; NRFHR=non-reassuring fetal heart rate patterns

This result was consistent with the previous studies in Australian and Uganda population (8.1 and 28 per 1,000 live births, respectively)[9,11].

NRFHR, preterm birth and difficult delivery were the risk factors associated with LAS-5 neonate in both the all population group and the group of neonate GA of more than 34 weeks.

NRFHR has three times more risk to develop LAS-5. Clinical diagnosis of NRFHR is involved in prolonging the low Apgar score, which is similar to the previous studies[12]. Moreover, NRFHR can forecast the neonate status and the need for resuscitation. This shows that intrapartum fetal monitor is useful to detect potential fetal hypoxia for appropriate intervention.

The risk of LAS-5 rose four times in the preterm birth. Although IUGR looked as if it affects more the LAS-5 group than the LBW among neonate of GA of less than 34 weeks, further investigation is needed due to the limited number of cases in this study. Pulmonary hypoplasia, hypoglycemia, and infection seemed to be a factor in the low Apgar score in the preterm group[13]. The effect of lung immaturity and associated premature conditions were seen as interfering factors. When the authors focused on late preterm neonate, they had three times more risk for LAS-5. The benefit of tocolytic therapy and steroid prescription in this group will be a challenging issue in the future.

Difficult delivery comprised of dystocia, failure or prolong instrumental delivery, and impacted fetal head at cesarean section. It had four times more risk for LAS-5 neonate. This should be one of the correctable factors. A 16-year of case review reported a neonatal birth asphyxia rate after shoulder dystocia of 8.6%[14]. Moreover, head-to-body delivery interval of five minutes or more increases the risk of severe acidosis and low Apgar score[15]. On the contrary, Ghidini et al reported that vacuum-assisted delivery was not an independence risk factor for LAS-5[16].

Interestingly, a prior study identified low maternal socio-economic status and public health insurance as risk factor for LAS-5[12]. This may be surrogated for other risk factors such as smoking, illicit drug use, and alcohol consumption[12]. Unfortunately, the present study was retrospective and had limited data of only public health insurance. A future combined measurement of health insurance and other substitute factors will be of value in health promotion and preventive policy.

Moreover, neonatal hypoglycemia is one of outstanding adverse neonatal outcome. Identifying fetal at risk for neonatal hypoglycemia should be of benefit. The characteristics of infants at risk such as macrosomia, infant of diabetes mother, prematurity, and temperature instability should be closely observed.

The present study had a limitation on analyzing only the low 1-minute Apgar score population while most previous studies compared with non-asphyxia neonatal group or normal Apgar score neonate. It limited the ability to compare results with other studies.

A multidisciplinary team is required to reduce the rate of low Apgar score. Good pre-conceptive evaluation (maternal medical and nutritional status), optimizing ANC, intra-partum high risk identification, accessible emergency operative theater, appropriate neonatal resuscitation team, and long-term strategy for growth and development of neonatal evaluation will become the future hospital service plan.

In conclusion, the prevalence of LAS-5 in

Prapokklao Hospital during the study period was 7.98 per 1,000 live births. Pregnancy together with NRFHR, preterm birth, and difficult delivery should be closed observed and planned to have neonatal resuscitation.

Further prediction model to identify fetal at risk of LAS-5 group will be useful.

What is already known on this topic?

Apgar score is a tool for evaluate the neonatal condition after birth. The 1-minute Apgar score is a representative for the requirement of immediate resuscitate, likewise 5-minute score implies the effectiveness of resuscitative efforts and is related to a higher risk of neurodevelopmental disability. There is limited data for low 5-minute Apgar neonate in the Thai population.

What this study adds?

The authors introduced another point of view in Apgar score area, which included only neonates with an Apgar score or seven or less at 1-minute and compared at 5-minute Apgar score. The present study demonstrated the incidence and risk characteristics of a continued low 5-minute Apgar score neonates. To reduce the bias, sub-group analysis in 34 gestation weeks or older was performed and found that the four independence risk characteristics were consistent with the all included population.

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Conflicts of interest

The authors declare no conflict of interest.

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