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Low Apgar Score and Mortality in Extremely Preterm Neonates Born in the United States

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Abstract

Aim—To investigate the relationship between low Apgar score and neonatal mortality in preterm neonates.

Methods—Infant birth and death certificate data from the U.S. National Center for Health Statistics for 2001–2002 were analyzed. Primary outcome was 28 day mortality for 690,933 neonates at gestational ages 24–36 weeks. Mortality rates were calculated for each combination of gestational age and five-minute Apgar score. Relative risks of mortality, by high vs. low Apgar score, were calculated for each age.

Results—Distribution of Apgar scores depended on gestational age, the youngest gestational ages having higher proportions of low Apgar scores. Median Apgar score ranged from 6 at 24 weeks, to 9 at 30–36 weeks gestation. The relative risk of death was significantly higher at Apgar scores 0–3 vs. 7–10, including at the youngest gestational ages, ranging from 3.1 (95% confidence interval 2.9, 3.4) at 24 weeks to 18.5 (95% confidence interval 15.7, 21.8) at 28 weeks.

Conclusion—Low Apgar score was associated with increased mortality in premature neonates, including those at 24 to 28 weeks gestational age, and may be a useful tool for clinicians in assessing prognosis and for researchers as a risk prediction variable.

Keywords

Apgar score; Neonatal mortality; Prematurity

Introduction

Dr. Virginia Apgar created the 10-point Apgar score more than 50 years ago to facilitate evaluation of newborns.(1) She proposed a score that could "... be used as a basis for discussion and comparison of the results of obstetric practices, types of maternal pain relief and the effects of resuscitation."(1) Although there has been some controversy surrounding its use, her scoring system continues to be used throughout the world.

Low Apgar scores were associated with mortality in studies conducted soon after the score was put into use, and in more recent cohorts.(2–5) A potential limitation of the Apgar score is its use in preterm neonates, whose scores may be depressed based on their immaturity,

even when they are relatively healthy.(6-7) A recent study confirmed the heterogeneity of Apgar score assignment in premature infants at different centers.(8) The design of the Apgar score is not optimal for use in prognostic models for several reasons, including its potential lack of reliability, and the likelihood that each of the five components carries different clinical significance despite having the same weight in scoring.(9)

Nevertheless, investigators have shown that the Apgar score may be a relevant factor in predicting mortality in preterm infants as early as 25 weeks gestational age, particularly when the score was very low (0 to 3).(4,10-11) One study was limited to Scandinavian newborns at 25 weeks gestation.(10) A second study reported the experience from a single U.S. hospital.(4) A recent population-based study reported that Apgar score at five minutes could predict mortality in neonates with low birth weight, particularly birth weights from 1,500 to 2,499 grams, although less predictably for infants with birth weight < 1,500 grams.(12) Due to the lack of data in preterm infants, a joint statement from the American Academy of Pediatrics and the American College of Obstetricians and Gynecologists declared, "Because there are no consistent data on the significance of the Apgar score in preterm infants, in this population the score should not be used for any purpose other than ongoing assessment in the delivery room."(13)

In light of its many potential limitations, we were interested in exploring the Apgar score's utility as a marker of severity of illness in preterm neonates, both as a possible guide for prognostic counseling as well as for research. The objectives of our study were to characterize the distribution of Apgar scores for US newborns born preterm, particularly those infants at the youngest gestational ages of 24 to 28 weeks, and to determine if the Apgar score added any significant information to gestational age with respect to neonatal mortality. We studied the U.S. preterm population for the years 2001 and 2002 and assessed the distribution of five minute Apgar scores and the relationship between five minute Apgar score and neonatal mortality at each week of gestation.

Patients and Methods

We used the US Birth Cohort Linked Birth and Infant Death Certificate data sets of 2001 and 2002, representing the years most recently available from the National Center for Health Statistics (NCHS) in which individual birth and death certificates were successfully linked.(14-15) In this cohort, there were 938,303 singleton live births to US residents with gestational age 24 to 36 and 6/7 weeks. The gestational age reported in NCHS data sets was derived from calculations based upon the last menstrual period. On some records, a month and year, but no day of last menstrual period was recorded. According to NCHS procedures, the gestational age was imputed in these circumstances by assigning the same gestational age as the preceding record with complete last menstrual period date having the same months of gestation (6.8% of the analytic cohort).(16-17) The Apgar score is not recorded on California and Texas birth certificates and the 194,840 infants born in those states were excluded. We further excluded 19,770 (2.7%) infants noted to have congenital anomalies. In order to minimize inaccurate dating and classification of gestational age, we excluded 29,648 neonates whose birth weights were at the extremes, less than the 1st percentile or greater than the 99th percentile according to published norms.(18) Of the remainder, 3,112 (0.45%) did not have five minute Apgar score recorded. The final study cohort included 690,933 infants.

All states had uniform reporting requirements of demographic and medical factors. Various states did not report specific items. Of the variables relevant to our analysis, only congenital anomalies were not reported in one state (New Mexico). For more detailed information

regarding completeness of data by state, refer to the Technical Appendix from the Vital Statistics of the United States.(16-17)

Median values and distribution of five minute Apgar scores were calculated for each gestational age group. The primary outcome variable was neonatal mortality, defined as death at or before 28 days of age. Using five-minute Apgar score as the predictor variable, neonatal mortality was calculated for the whole cohort and then for each gestational age week. Relative risk of neonatal mortality for Apgar score 0-3 vs. 7-10 was calculated with 95% confidence intervals.

Using receiver operating characteristic (ROC) curve analysis, area under the curve was estimated for the outcome of neonatal mortality, using the following as predictors: gestational age alone, five minute Apgar score alone, and a model combining gestational age and Apgar score. Analyses were computed using SAS 9.1 (SAS, Cary, NC). This study was approved by the Stanford University Institutional Review Board.

Results

Distribution of Apgar scores depended on gestational age, with the youngest gestational ages having higher proportions of low Apgar scores (Table 1). At higher gestational ages, beyond 30 weeks, more than 90% of neonates had Apgar scores 7-10. In contrast, at the youngest gestational ages of 24-26 weeks, less than 70% of neonates had scores 7-10. The median five-minute Apgar score was 6 for 24 weeks gestation, 7 for 25-26 weeks gestation, and 8 for 27-29 weeks gestation, compared to 9 for 30-36 weeks gestation. Results were similar across all states in the study.

Neonatal mortality was higher at lower Apgar scores at each gestational age (Table 1). The relative risk of neonatal death for Apgar score 0-3 vs. 7-10 ranged from 3.1 (95% CI 2.9, 3.4) at 24 weeks gestational age to 18.5 (95% CI 15.7, 21.8) at 28 weeks. The relative risk of mortality associated with low vs. high Apgar was significantly higher for increasing gestational age (Table 1).

Mortality rates according to individual five-minute Apgar scores are shown for selected gestational ages in Table 2 and Figure 1. For neonates at all gestational ages, including 24-25 weeks, Apgar score of 9 or 10 was associated with mortality rates less than 10%. On the other hand, Apgar score of 1 was associated with the highest mortality rates, 38% - 50% for the higher gestational ages 33 to 36 weeks, and up to 84.1% for 24 weeks gestation. For each gestational age group, there was a stepwise increase in mortality for each 1 point in decreasing Apgar score, with a break point at Apgar score of 3, below which mortality increased at a steeper rate. However, an exception to this pattern was mortality at Apgar score of 0. While mortality at Apgar score of 0 was lower than at a score of 1 for the entire cohort, this pattern was most pronounced at older gestational ages, was less prominent with decreasing gestational age, and was not seen at 24 weeks (Table 2, Figure 1).

Using ROC curve analysis, area under the curve for the prediction of neonatal mortality was 0.90 for gestational age alone, 0.90 for five minute Apgar score alone, and 0.94 when gestational age and Apgar score were both considered in the prediction model.

Discussion

In our analysis of a national cohort of preterm neonates born from 2001 to 2002, we found that low five-minute Apgar score was associated with neonatal mortality at all gestational ages from 24 to 36 weeks. The area under the curve in ROC analysis was similar for gestational age and Apgar score. The addition of Apgar score to gestational age increased

the area under the curve in ROC analysis, increasing the ability to predict mortality. Although there was higher incidence of low Apgar scores at lower gestational ages, even at 24 weeks, 46.3% of infants had scores of 7-10. Lower Apgar scores were associated with a higher risk of neonatal mortality across all ages. The magnitude of this relative risk increased for the higher gestational age groups.

The subjectivity that is necessarily part of assignment of Apgar score may limit its utility in clinical practice, particularly for premature infants. The joint statement from the American College of Obstetricians and Gynecologists and the American Academy of Pediatrics notes that it may be inappropriate to use the Apgar score alone to diagnosis birth asphyxia or predict neurologic outcome, and that the Apgar score of an infant during resuscitation is not equivalent to a score of a spontaneously breathing infant.(13) There is inconsistency and variability in assigning the Apgar score, particularly for resuscitated infants.(19-22) A physician assigning Apgar scores may often do so retrospectively after the period of intense clinical management, thus decreasing its utility. Despite these limitations, which would seemingly tend to weaken the association between Apgar score and clinical outcome, we nonetheless found a robust relationship between Apgar score and death. Other investigators have also established the utility of the standard Apgar score at both one and five minutes as a predictor of outcome in neonates as young as 25 weeks gestational age.(4,10,23-24)

Assignment of a low Apgar score is likely multifactorial, including antenatal and postnatal factors. The score may reflect an underlying condition or injury prior to birth. It could also reflect adequacy of resuscitation. In a case-control study of perinatal death and cerebral palsy, there was a small proportion of cases in which suboptimal response to a newborn's condition may have contributed to a poor prognosis.(25) In extremely preterm infants, a low Apgar score may represent a parental and physician decision to withhold resuscitation for what was considered a pre-viable patient; a self-fulfilling prophecy. Future study could focus on the contribution of such factors to the relationship between low Apgar score and mortality.

At each gestational age we found a breakpoint at Apgar score of 3, with a steeper increase in mortality at Apgar scores of 2 and 1. However, especially at older gestational ages, there was a paradoxical decrease in mortality for Apgar score of 0 compared with a score of 1. One possibility for this finding is that some neonates who initially showed signs of life, but deteriorated to an Apgar score of 0 at five minutes and failed to respond to resuscitation, may have been recorded as stillbirths. In contrast, all neonates with an Apgar score of 1 at five minutes would have been recorded as a live birth and would have been included in this analysis even if they died in the delivery room.

Our study was of U.S. birth certificate data, which would be collected and recorded differently by state. However, we did find similar results across states. It should also be noted that our findings may not be applicable to developing countries where both the recording of Apgar scores as well as premature neonatal survival could be considerably different than the United States.

With decreasing gestational age, mortality increased across the entire range of Apgar scores. As overall mortality increased, the relative risk of neonatal death for low vs. high Apgar score decreased (Table 1). While the extent of the relative risk diminished, even at 24 weeks the relative risk of mortality between low vs. high Apgar score infants was 3.1. We suspect that the decreasing impact of low Apgar score on very preterm infants is partly due to the higher mortality from multiple causes seen for that population. A very preterm infant has a higher risk of mortality even if appearing well in the immediate newborn period. On the other hand, for term and late preterm infants with relatively high survival rates, the

circumstance related to mortality are more likely to be associated with low Apgar scores. However, it is interesting to note that even for the most preterm infants, an Apgar score of 7-10 is associated with relatively high survival (Table 1).

In counseling parents of premature newborns soon after delivery, clinicians often use gestational age or birth weight as a guide for prognosis. A recent study highlights that factors in addition to gestational age can help to predict outcome in very premature neonates.(26) The addition of five-minute Apgar score to gestational age could help to better quantify risk prediction for clinicians. For example, a neonate born at 24 weeks with Apgar score of 2 would have a 2-fold higher risk of mortality (67.8% vs. 32.6%) than the “average” baby born at the same age with median Apgar score of 6. Conversely, a 24-week gestation neonate with Apgar score 8 or 9 would have a 2-fold decreased risk of mortality than the “average” 24-week neonate.

A limitation of our study is that we do not have breakdowns of various components of the Apgar score to see which component may be the most clinically relevant, i.e. breathing or lack of tone. Another limitation of our study is that we did not investigate the potential interactions of other demographic and clinical factors other than gestational age which may impact the relationship between Apgar score and mortality. The contribution of the Apgar score to more complex prediction models, including factors such as gender, race, maternal, and clinical factors was beyond the scope of the current study and is worthy of further investigation. Although the Apgar score has not been well tested as a predictor of mortality in premature neonates, it continues to be used as one of the variables in risk adjustment when comparing mortality rates for preterm neonates, often as part of a score such as the Score for Neonatal Acute Physiology – Perinatal Extension or Vermont Oxford Network Risk Adjustment.(27) Our study results suggest that this is a reasonable practice.

In summary, we found that the five-minute Apgar score was associated with preterm neonatal mortality for infants born as early as 24 weeks. Although recognized standards for scoring resuscitated neonates could potentially increase its utility, our findings based on the standard approach may help to inform clinicians taking care of premature neonates regarding decisions based on prognosis. The findings also support the continued use of Apgar score as a predictor variable in preterm infant research and risk adjustment.

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Abbreviations

NCHS	National Center for Health Statistics
CI	Confidence interval
ROC	Receiver Operating Characteristic

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Figure 1. Mortality at 28 days by 5 minute Apgar score for selected gestational ages. Data source: National Center for Health Statistics. 2001, 2002 Birth Cohort Linked Birth and Infant Death Data Set. Unweighted R-square for 24 weeks: 0.92; 28 weeks: 0.83; 36 weeks: 0.58.

Table 1
Distribution of 5-minute Apgar scores and neonatal mortality rate (NMR) per 1000 live births by gestational age

Gestational age (weeks)	N	5-minute Apgar score						RR mortality 0-3 vs. 7-10 (95% CI)
		0-3		4-6		7-10		
		Distribution (%)	NMR	Distribution (%)	NMR	Distribution (%)	NMR	
24	5466	23.8	732	29.9	361	46.3	234	3.1 (2.9, 3.4)
25	6357	13.6	635	27.1	240	59.3	136	4.7 (4.2, 5.1)
26	7281	9.3	519	23.3	159	67.4	83	6.2 (5.5, 7.0)
27	8170	5.9	467	17.9	114	76.3	47	9.9 (8.5, 11.4)
28	12415	3.6	428	12.3	95	84.1	23	18.5 (15.7, 21.8)
29	12024	3.0	397	10.7	83	86.3	20	20.1 (16.7, 24.2)
30	17038	1.9	393	8.4	63	89.7	9	41.4 (33.5, 51.1)
31	23692	1.2	262	5.5	46	93.3	5	49.9 (38.1, 65.3)
32	34373	0.8	338	3.9	44	95.2	3	109.5 (85.0, 141.1)
33	52030	0.5	292	2.8	42	96.7	2	118.4 (91.8, 152.8)
34	90986	0.4	282	2.0	34	97.7	2	168.4 (133.5, 212.4)
35	151872	0.3	227	1.4	29	98.3	1	176.2 (140.4, 221.1)
36	269229	0.2	163	1.0	21	98.8	1	196.5 (154.4, 250.1)
All	690933	0.9	468	3.1	100	96.0	5	93.9 (89.0, 98.0)

RR = relative risk; CI = confidence interval

Table 2

Neonatal mortality rate per 1000 live births by 5-minute Apgar score and gestational age

5-minute Apgar score	Gestational age (weeks)				
	24	25	26	27	28
10	91	83	30	0	9
9	165	111	60	30	10
8	226	122	82	47	26
7	275	167	105	71	53
6	326	206	131	83	65
5	382	272	167	146	127
4	434	313	246	188	176
3	425	406	326	246	184
2	678	587	497	358	423
1	841	775	636	676	610
0	876	719	573	549	554

Mortality is expressed as number of deaths prior to 28 days per 1000 live births. For example, neonates at 25 weeks gestational age with Apgar score of 9 had mortality rate of 111 deaths per 1000 live births.